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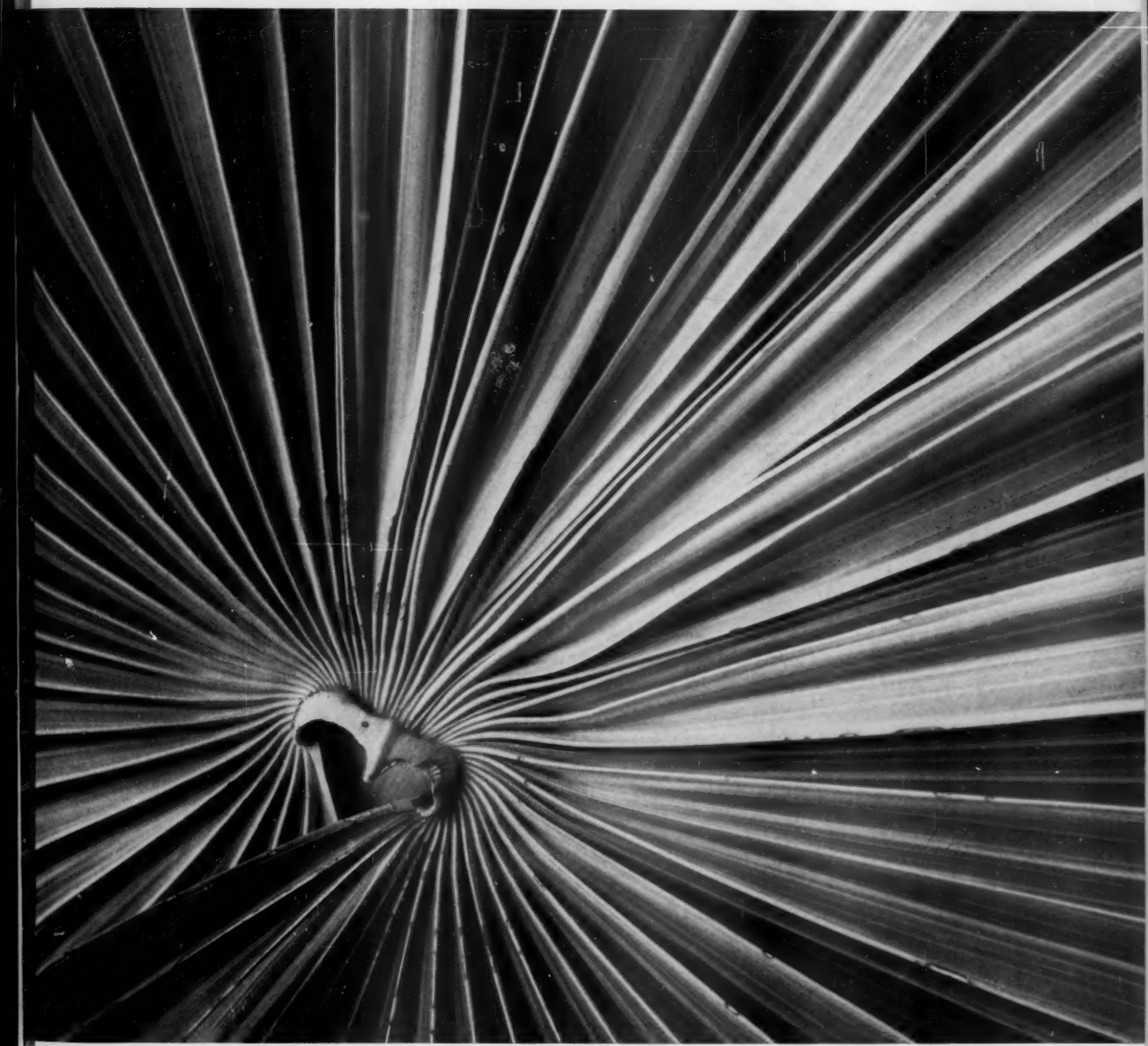

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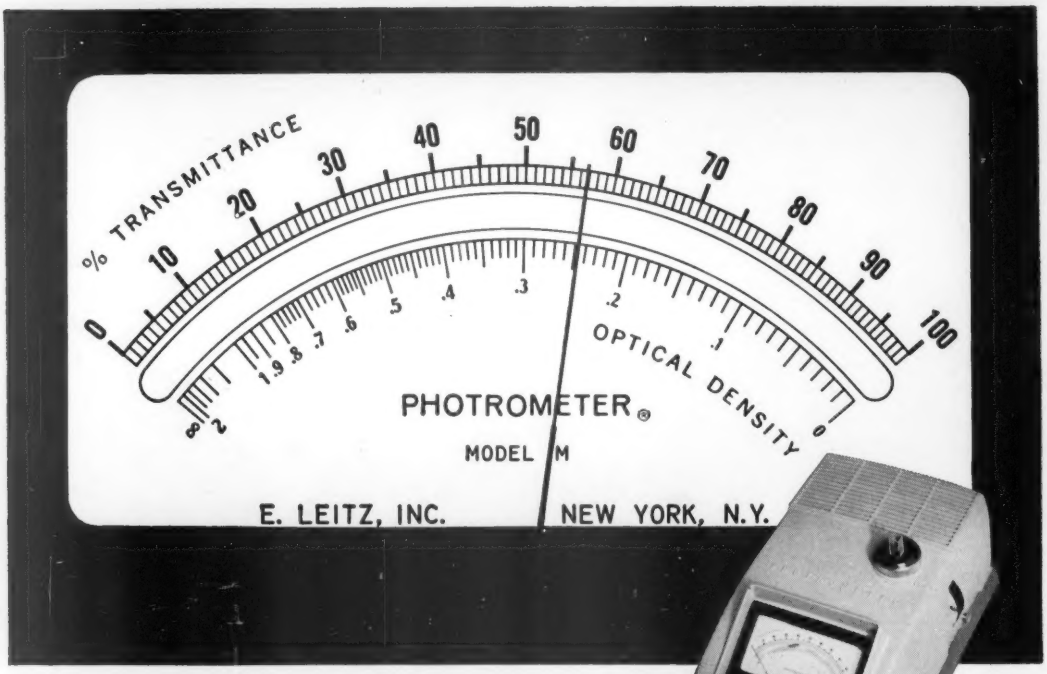

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SCIENCE

Editorial Irony Compounded 301

Articles Immunological Tolerance: *P. B. Medawar* 303
The phenomenon of tolerance provides a testing ground for theories of the immune response.

Immunological Recognition of Self: *F. M. Burnet* 307
Such recognition suggests a relationship with processes through which functional integrity is maintained.

Limitations on Space Flight due to Cosmic Radiations: *H. J. Curtis* 312
Newly discovered radiations dictate vehicle design and orbit of future manned space flights.

Science in the News A Few Headaches: Priorities for Science; Preparing for the Test Ban Talks; the Rules Committee 317

Book Reviews C. H. Waddington's *The Ethical Animal*, reviewed by *T. Dobzhansky*; other reviews 323

Reports Painless Killing of Crabs and Other Large Crustaceans: *G. Gunter* 327

Depression of Taste Sensitivity to Specific Sugars by Their Presence during Development: *D. R. Evans* 327

Pliable, Root-Permeable Layers for Separation of Portions of Experimental Plant Root Systems: *J. F. Stone* and *J. R. Mulkey, Jr.* 329

Effect of Mitomycin C on Lateral Root-Tip Chromosomes of *Vicia faba*: *T. Merz* 329

Sensory Deprivation and Pain Thresholds: *J. Vernon* and *T. E. McGill* 330

Selective Viral and Rickettsial Serum Antibody Absorption by a Chromatographic Column: *N. K. Brown* 331

A "D"-like Antigen in Rhesus Red Blood Cells and in Rh-Positive and Rh-Negative Red Cells: *P. Levine* et al. 332

Effect of Strychnine upon the Electrical Activity of an Isolated Nerve Cell: *Y. Washizu, G. W. Bonewell, C. A. Terzuolo* 333

Departments Forthcoming Events; New Products 336

Cover Portion of a leaf of the palm *Thrinax parviflora* in Fairchild Tropical Garden, Miami, Fla. See page 325. [W. H. Hodge, Longwood Gardens, Kennett Square, Pa.]

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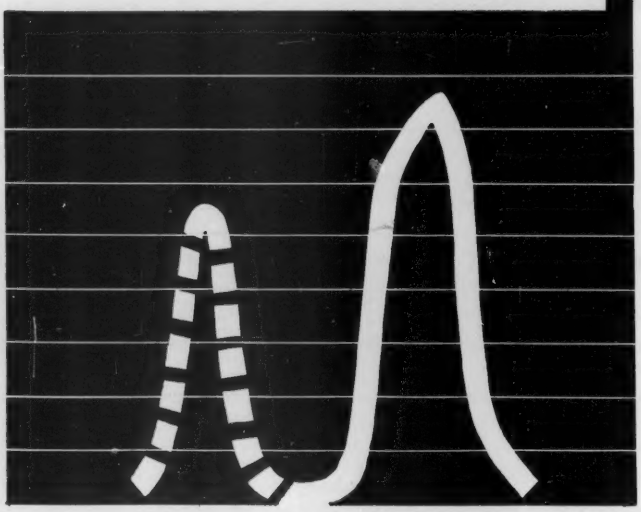

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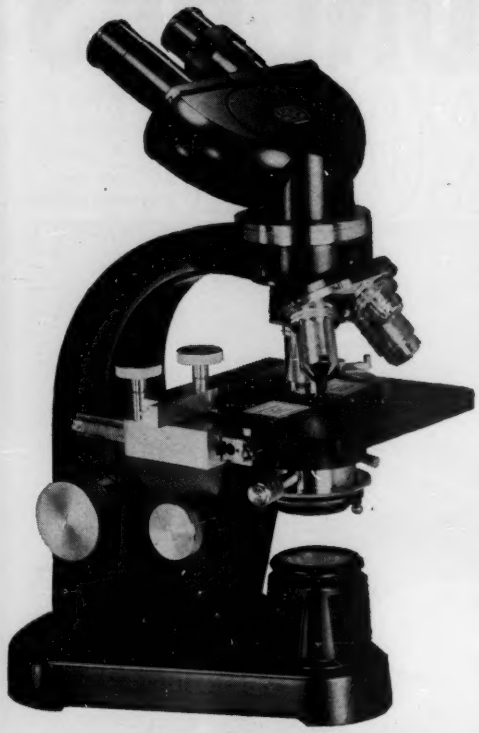

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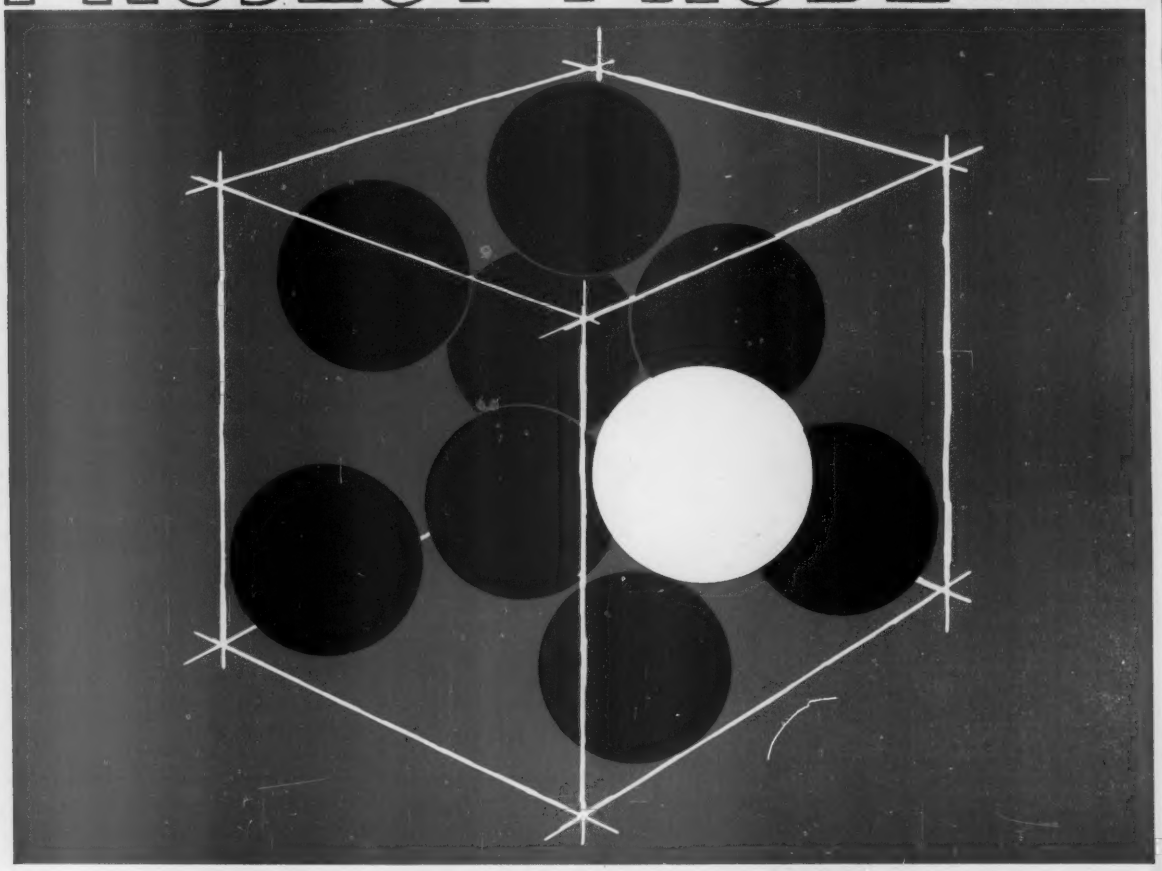

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Irony Compounded

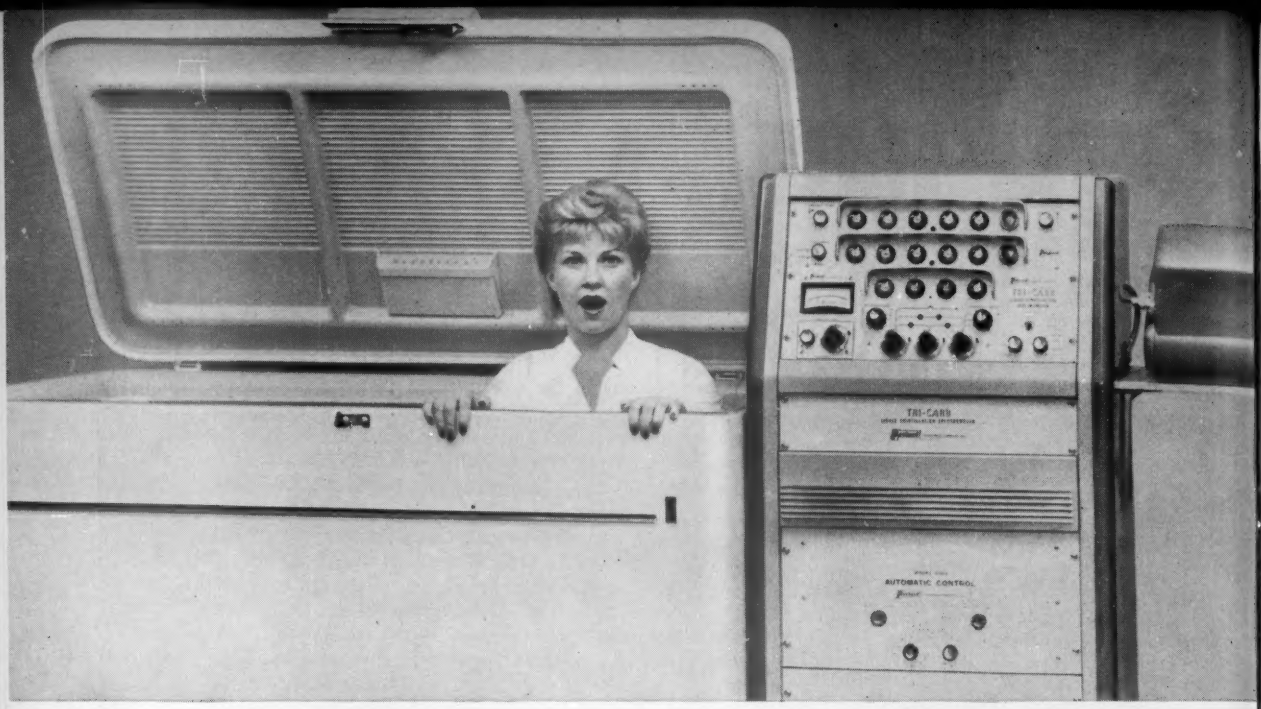
There is irony in the circumstance that the present overhauling of American education is being led in good part by the sciences, for one of the thinkers whose work helped produce the view of education under attack, John Dewey, was himself much influenced by science, and this influence is reflected in his educational doctrines. To simplify a complex matter, the change sought is from a learner-centered curriculum, favored by many professional educators, toward a subject-centered curriculum, favored by lay critics of education. In the effort at overhaul, Dewey has sometimes been taken as the symbol of what is wrong with education, but at least some of the readers of his views on science would find this symbol poorly chosen.

Dewey was one of the most prolific of writers, but certain key ideas run through much of what he wrote. He saw science as *the* method of finding things out. In his interpretation of science, he was at pains to elaborate the view that scientific inquiry does not begin with the gathering of data. Rather it begins with a problem, a conflict, a difficulty. The problem suggests a possible solution, or hypothesis, and it is this hypothesis that guides the gathering of data. The data then serve to prove or disprove the hypothesis, and to solve or leave unresolved the problem. Such, very briefly, was Dewey's vision of science, a vision reflected in his educational doctrines. He was opposed to authoritarianism and believed in inculcating an experimental attitude in students. Emphasis in education was to be on method, on solving problems.

At the same time, Dewey's interpretation of science has been the subject of some criticism by scientifically oriented thinkers. Another theme running through much of his work, motivated perhaps by his great concern with social and moral matters, is his attack on "dualisms," such as the one he saw existing between theory and practice, between intelligence and conduct. This attack, so the criticism runs, has resulted in a view of science in which scientific problems arise too immediately out of practical problems, and in which the solution to scientific problems is tied too closely to the solution of practical problems. According to the critics, not all distinctions are "dualisms," and the truth of the matter is that scientific activity is related to a much wider universe than the one we meet in daily life. Astronomy is a bigger subject than navigation.

This misinterpretation of science introduces a second note of irony in the bearing of Dewey's thought on present educational tendencies. If we are to be guided in education by the values of science, and if science does make reference to this wider universe, then, so the criticism concludes, education must find a place for disinterested curiosity and understanding. Education should foster a love of subject matter for its own sake. True, the occurrence of a storm can be used in the classroom to initiate a discussion of climatic conditions in the United States, but pedagogy so conceived has its limits.

Two wrongs, of course, do not make a right, nor does irony compounded cancel itself out. A moral is suggested, however. If some of the partisans of a subject-centered curriculum too readily take Dewey as the philosopher of all they oppose, then some of our professional educators are equally hasty when they make Dewey into a philosopher who is above reproach.—J.T.



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Immunological Tolerance

The phenomenon of tolerance provides a testing ground for theories of the immune response.

Peter Brian Medawar

"Immunological tolerance" may be described as a state of indifference or nonreactivity towards a substance that would normally be expected to excite an immunological response. The term first came to be used in the context of tissue transplantation immunity—that is, of the form of immunity that usually prohibits the grafting of tissues between individuals of different genetic make-up—and it was used to refer only to a nonreactivity caused by exposing animals to antigenic stimuli before they were old enough to undertake an immunological response. For example, if living cells from a mouse of strain CBA are injected into an adult mouse of strain A, the CBA cells will be destroyed by an immunological process, and the A-line mouse that receives them will destroy any later graft of the same origin with the speed to be expected of an animal immunologically forearmed. But if the CBA cells are injected into a fetal or newborn A-line mouse, they are accepted; more than that, the A-line mouse, when it grows up, will accept any later graft from a CBA donor as if it were its own. I shall begin by using the term *immunological tolerance* in the rather restricted sense that is illustrated by this experiment and shall discuss its more general usage later on.

The experiment I have just described (*1*) can be thought of as an artificial reproduction of an astonishing natural curiosity, the phenomenon of red-cell chimerism in certain dizygotic twins. The blood systems of twin cattle before birth are not sharply distinct from each other, as they are in most other twins; instead, the blood systems make anastomoses with each other, with the result that the twins can indulge in a prolonged exchange of blood before birth. In 1945, R. D. Owen (*2*) made the remarkable discovery that most twin cattle are born with, and may retain throughout life, a stable mixture—not necessarily a fifty-fifty mixture—of each other's red cells; it followed, then, that the twin cattle must have exchanged red-cell precursors, and not merely red cells, in their mutual transfusion before birth. This is the first example of the phenomenon we came to call immunological tolerance; the red cells could not have "adapted" themselves to their strange environment because they were in fact identified as native or foreign by those very antigenic properties which, had an adaptation occurred, must necessarily have been transformed. A few years later R. E. Billingham and I (*3*), with the help of three members of the scientific staff of the Agricultural Research Council, showed that most dizygotic cattle twins would accept skin grafts from each other, and that this mutual tolerance was specific, for skin transplanted from third parties was cast off in the expected fashion. We did not set out with the idea of studying the immunological consequences of the phenomenon described by Owen; on the contrary, we had been goaded by H. P. Donald into trying to devise a foolproof method of distinguishing monozygotic from dizygotic twins, an enterprise that seemed reasonable enough against the rather thorough background of knowledge we already possessed about the behavior of skin grafts in experimental animals (*4*). It was F. M. Burnet and F. Fenner (*5*) who first read a general significance into Owen's discovery and who wove it into a general hypothesis of the immunological response which counted the phenomenon of tolerance among its theoretical consequences.

In the outcome, it proved impossible to distinguish between the two kinds of twins by skin grafting, but the causal connection between Owen's phenomenon and our own was obvious, and we were now confident of our ability to make adult animals accept tissue homografts by reproducing in the laboratory the very state of affairs that had come about by natural accident in twin cattle. Billingham, L. Brent, and I eventually succeeded in doing this, and our first report on the matter was published in 1953 (*1*). In the meantime, M. Hašek (*6*), working against an entirely different conceptual background, had reproduced Owen's phenomenon in chickens by the ingenious method of making a deliberate synchorial parabiosis between chick embryos in the shell. At hatching the parabionts separated, and from then on they were incapable of making antibodies against each other's red cells, or, as later work showed (*7*), of rejecting grafts of each other's skin. It is now known that chimerism can occur naturally, though rarely, in twin sheep, and more rarely still in twin human beings (*8*); in twin chickens it is

Dr. Medawar is professor of zoology at University College, London, England. This article is the lecture he delivered in Stockholm, Sweden, on 12 December 1960, when he received the Nobel prize in medicine and physiology for 1960, a prize which he shared with Sir Macfarlane Burnet. It is published with the permission of the Nobel Foundation. The text of the address is also appearing in *Nature*. Dr. Burnet's lecture appears on page 307 of this issue.

probably the general rule. That chimerism should occur in man is clear proof that the principle of tolerance applies to human beings as well as to laboratory animals, and human chimeric twins can accept grafts of each other's skin (*9*).

Properties of the Tolerant State

The main points that emerged from our analysis of the tolerant state were these. In the first place, tolerance must be due to an alteration of the host, not to an antigenic adaptation of the grafted cells, for grafts newly transplanted in adult life have no opportunity to adapt themselves, and the descendants of the cells injected into fetal or newborn animals can be shown, by N. A. Mitchison's methods, to retain their antigenic power (*10*). Once established, the state of tolerance is systemic; if one part of the body will tolerate a foreign graft, so will another; we found no evidence that a tolerated graft builds up a privileged position for itself within its own lymphatic territory. The stimulus that is responsible for instating tolerance is an antigenic stimulus—one which, had it been applied to older animals, would have caused them to become sensitive or immune. A plural stimulus can induce plural tolerance; the donor will usually possess several important antigens that are lacking in the recipient, and long-lasting tolerance must imply tolerance of them all. The state of tolerance is specific in the sense that it will discriminate between one individual and another, for an animal made tolerant of grafts from one individual will not accept grafts from a second individual unrelated to the first; but it will not discriminate between one tissue and another from the same donor. The injection of leucocytes or lymphoid cells can confer tolerance of skin grafts, for example, and later work has shown that the same is true for grafts of thyroid tissue, ovary, kidney, and adrenal gland. These various tissues do indeed differ in their antigenic make-up, but not, apparently, in respect of antigens that play an important part in transplantation immunity. If leucocytes lacked some important antigen present in skin, it is difficult to see how they could confer tolerance of skin, and P. L. Krohn, using more direct and more critical methods, has found it impossible to distinguish between the antigenic make-up, so far as it governs their transplantability, of ovary and skin (*11*).

Tolerance can be brought promptly and permanently to an end by an experimental device which combines certain principles established by N. A. Mitchison and M. W. Chase. Please cast your mind back to the model experiment I described at the beginning of this article and imagine an A-line mouse which is tolerant of CBA tissue and which carries a CBA skin graft as outward evidence that this is the case. The tolerated CBA graft can be destroyed within a week by injecting into its host cells from A-line mice which have reacted upon and rejected CBA tissues in the expected fashion. A less spectacular but in some ways more informative variant of this "adoptive immunization" is the injection of the tolerant mouse with lymphoid cells from A-line mice that have *not* been sensitized beforehand by CBA tissues. Here too, though much more slowly, the tolerant state is brought to an end. The inference we drew from this experiment —and nothing has occurred since to make us question it—was that tolerance is due to a central failure of the mechanism of immunological response and not to some intercession at a peripheral level.

There is one important question about tolerance which the experimental system I have been describing is very ill equipped to answer: Does the maintenance of the tolerant state depend upon the continuing presence of the antigen that provoked it? When living cells are used to procure tolerance they survive into adult life and therefore maintain a chronic antigenic stimulus, but is it necessary that they should do so? So far as transplantation immunity is concerned, no completely confident answer can be given until the antigens that excite it can be extracted in a sufficiently potent form; but with "tolerance" of foreign proteins and red cells, it does indeed seem that antigen must continue to be present, even though in quantities below the threshold of direct estimation, if a fully nonreactive state is to be maintained (*12*).

This is one of the most important single pieces of evidence that must be taken into consideration when devising hypotheses to account for tolerance, and it points to the clear distinction that must be drawn between the dosages of antigen necessary, on the one hand, to instate tolerance and, on the other hand, to maintain it. Much else is still uncertain—for example, the significance to be attached to the "partially tolerant" state. Tolerance is not an all-or-nothing phenomenon; every degree of tolerance is to be found, from that which allows a graft to live just perceptibly longer than would be expected of it in a normal animal to that in which the graft is permanently accepted by and incorporated into its host. Is an animal partially tolerant because all its reactive cells are almost completely debilitated, or because, while most of them are completely out of action, a minority retain full possession of their powers?

Tolerance and Runt Disease

It has been the experience of all laboratories that tolerance is most easily procured by injecting lymphoid cells into immature animals. This is not because lymphoid cells are in themselves more strongly antigenic than others—there is evidence that they are not—but probably because they are distributed throughout the body of the animal into which they are injected. This should make them adept at producing tolerance; an animal can be immune when only a minority of the cells that are competent to react immunologically are doing so, but it cannot be tolerant unless the very great majority of them are not.

Unfortunately, the lymphoid cells used to induce tolerance are immunologically qualified to attack the tissues of their host, with consequences that were first revealed by Billingham and Brent (*10*) and, in a somewhat different form, by M. Simonsen (*13*). The injection of foreign adult lymphoid cells into newborn mice of an unrelated strain gives rise to a fatal or chronic illness, "runt disease," marked by retardation of growth and widespread damage to the host's lymphoid tissue. Its discoverers have proved beyond question that runt disease is immunological in origin. So far as it concerns mice, the clear recognition of runt disease had to await the development of a technique for injecting newborn mice intravenously (*14*); until that had been done, there was every inducement to believe that death or stunting was due to accidental damage caused by injecting cells into mice *in utero*.

Runt disease or splenomegaly (one of its earlier symptoms) provides a test of the immunological competence of cells and lends itself to exact studies of their immunological capabilities; perhaps the most important discovery that can be

credited to it is that of the presence of an immunologically competent cell in peripheral blood. The aspect of runt disease that concerns us here is its relationship to tolerance. A state of tolerance must obviously abet the onset and probably the progress of runt disease, because if adult lymphoid cells are to attack the tissues of the animal into which they are injected they must live long enough to be able to do so. The frequency with which runt disease was associated with the induction of tolerance gave rise to the suspicion that tolerance might itself be a pathological condition. Might not the adult lymphoid cells used to induce it simply exterminate the developing lymphoid cells of the host and take their place? This cannot be so. Tolerance unaccompanied by any symptom of runt disease is produced by the injection of embryonic cells or by a natural or artificial parabiosis between embryos, and it leads in such instances to a stable chimerism in which native and foreign cells seem to coexist without the one ousting the other. It can be produced, moreover, by adult lymphoid cells which, though antigenically foreign to their hosts, are for simple genetic reasons incapable of attacking them. The experiment described at the beginning of this article is in fact best carried out by injecting, not adult CBA lymphoid cells, but adult lymphoid cells from a first-generation hybrid between mice of strains A and CBA. By and large there seems no reason to believe that tolerance can be explained in terms of cellular competition and replacement.

Other Forms of Immunological Nonreactivity

The antigenic substances I have so far had in mind are "foreign" only in the sense that they derive from other members of their recipients' species. Tolerance of more remotely foreign cellular antigens is more difficult but certainly not impossible to achieve. But even if we confine the concept to the reactions that take place within the compass of a species, it is clear that tolerance can be induced by antigens belonging to more than one chemical class and may extend to more than one modality of response. A tolerant animal not only fails to engage in the "cellular" type of response we associate with the reaction against homografts of skin; it fails equally to make humoral antibodies—for example, isohemagglutinins—and the antibodies that fail to make an appearance include those of so-called "natural" occurrence (for example, human anti-A or anti-B) as well as those that appear only in response to deliberate immunization. It is not surprising, then, that many authors (*15*) should have found that a state not yet formally distinguishable from tolerance is brought about by the injection of purified protein antigens into young animals.

Even in this wider sense tolerance is by no means the only kind of specific immunological nonreactivity (*16*). L. D. Felton described and named the phenomenon of "immunological paralysis" in 1949. Felton showed that adult mice could be immunized and therefore protected against otherwise lethal doses of living pneumococci by the injection of 0.5 microgram of a pneumococcal polysaccharide of the appropriate antigenic type. But, far from conferring resistance, the injection of larger doses (500 micrograms, for example) abolished it, for the mice became vulnerable to pneumococcal infection and could no longer be protected against it by an injection of the smaller dose.

An analogous phenomenon was discovered by F. J. Dixon and P. H. Maurer when they showed that large doses of soluble protein antigens failed to excite a response from adult rabbits. The foreign protein disappeared from the circulation at just the rate that would be expected if no antibodies against it had been formed. At one time most of us believed that immunological paralysis could not be classified as an essential nonreactivity. Antibodies were probably formed, we believed, but were promptly bound by antigen present in vast excess. But the most recent work, notably from A. H. Coons's laboratory, makes this interpretation rather doubtful, for refined methods have so far failed to reveal that any immunological reaction is in progress. These observations have given rise to the hope that paralysis and tolerance of soluble antigens are indistinguishable phenomena.

The problem now to be decided is whether or not the inception of tolerance in the narrower sense depends upon some quantitatively distinctive property of immature lymphoid cells. Are embryonic cells specially easy to paralyze, for example, or (this comes to the same thing) is it specially difficult to make adult cells tolerant? I know that work bearing on this problem is in progress in Coons's and Mitchison's laboratories. For many reasons—one of them the need to distinguish between the doses of antigen needed for the inception and the maintenance of the unresponsive state—the problem is by no means so easy to tackle as might appear at first sight.

It is a matter of some importance that a quantitative study of the same kind should be made of tolerance of foreign tissue grafts. To refer once again to the experiment described at the beginning of this article, we can be sure that an *adult* A-line mouse will not be made tolerant of CBA tissues by the injection into it of a proportionate multiple of the number of CBA cells that would have sufficed if the recipient had been newly born, but we still do not know whether a *dis*proportionately large number of CBA cells might not confer tolerance upon a mouse, say, 10 days old. However, the possibility that tolerance and paralysis are no more than quantitatively distinguishable, if even that, makes it more urgent than ever before to prepare the antigens that excite transplantation immunity in an adequately potent form.

Two other forms of nonreactivity should be mentioned. One is the specific tolerance of tissue grafts which may be conferred upon a totally irradiated mouse whose hematopoietic tissues have been restored by an injection of foreign bone-marrow cells. J. F. Loutit has suggested that the phenomenon is akin to tolerance in the narrower sense defined by our own experiments, but here, too, the analogy with immunological paralysis is not far to seek. Curiously enough, the encouragingly long survival times of kidney homografts reported by our surgical colleagues in Boston and Paris (*17*) have been brought about by the use of rather lower doses of whole-body irradiation than experience with mice might lead one to regard as essential. Perhaps the behavior of inbred and homozygous mice is not the best theoretical guide to what may be expected of animals so obstinately heterozygous as human beings. Is it possible that "radiation-induced tolerance" may be easier to secure when the mouse donors are hybrids of type X/Y and the recipients hybrids of type Y/Z? This model is also unrealistic, but more akin in principle to the genetic situation that human beings confront us with in real life.

Finally—I have put it last because

it is the least easy to classify, though it might turn out to be the paradigm of all such phenomena—I must mention the inhibition of drug allergy described by M. W. Chase and M. Sulzberger (*18*). Guinea pigs fed by mouth with, for example, picryl chloride no longer develop a cutaneous hypersensitivity of the delayed type upon the application of that substance to the skin. Analysis has shown that this, too, is an essential nonreactivity. Many of us nourish the hope that a similar principle might be turned to good account in transplantation immunity, if it should prove possible to prepare a "haptenized" derivative of the antigens that cause it to come about.

Biological Significance

Tolerance is a natural phenomenon, though its natural occurrence among chimeric twins may be something of an oddity. Has it any wider zoological significance?

The immunological defenses of the body are directed against foreign matter. It is not at all common for an animal to react upon the native ingredients of its own body. Burnet was the first to realize that this is not a state of affairs to be taken for granted but something that calls for a special explanation, and it was his attempt to explain it that led him to predict that antigens which impinged upon an animal sufficiently early in its life would come to be accepted as if they were its own. Now that tolerance is an established fact we may turn his argument the other way about. Tolerance is ideally well qualified to provide a built-in natural safeguard against the danger that an animal might be sensitized or immunized by the constituents of its own body, and this may turn out to be its biological *raison d'être* (*19*). If this argument is valid, then the only substances capable of exciting auto-immune reactions should be those which never normally have access to centers of immunological response, so that the body has no opportunity to learn to tolerate them. I do not know of any evidence that contradicts this inference.

Tolerance makes one think anew about the special relationship that holds between a mammalian mother and its unborn young. There are hints in the literature that a mammalian infant may be specially tolerant of antigens of maternal origin, and evidence of such a relationship should be found more readily among human beings than elsewhere, for, unlike rats and mice, we have a long gestation period, and unlike sheep and cattle, our fetal membranes are permeable by at least some molecules as large as proteins. Yet it seems most unlikely that maternally induced tolerance should be of regular or well-defined occurrence. The permeation of the fetus by foreign antigens gaining access through the mother might weaken its resistance in later life to infectious disease (we may recall here the significance read by Burnet and Fenner into Traub's observations on lymphocytic choriomeningitis) (*5*). This is only one among half a dozen reasons why traffic between maternal and fetal circulations should be under very close control. The occurrence of runt disease makes it of course unthinkable that the barrier between mother and fetus should be easily penetrable by anything so large as maternal cells.

Theories of Tolerance

Burnet and I have agreed upon a division of labor which absolves me from speculating upon the causes of the various kinds of essential nonreactivity I have described. Tolerance, like the secondary response and the nature of immunological "memory," has become something of a testing ground for theories of the immune response. It must be said that the occurrence of tolerance does not yet follow from any hypothesis of the nature of the immune response that has been verified by *independent* means. Far too much is still uncertain. We do not yet know whether any one antibody-forming cell is potentially capable of making any antibody within the organism's immunological repertoire or whether the competence of any one such cell is restricted to a subclass of the reactions that can be engaged in by the organism considered as a whole. We do not yet know whether the act of synthesis undertaken by an antibody-forming cell is strictly and specifically underwritten by the cell's genetic make-up or whether, in J. Lederberg's terminology, the instructions that govern that act of synthesis are imparted by the antigen itself. And if it should be true that the antigen does no more than choose between one set of pre-existing instructions and another, we still do not know whether those instructions are already present in the zygote, and therefore part of the legacy of its descendants, or whether they must be added to (by mutation, necessarily) during the course of growth. Finally, we do not even know whether the antitheses, as I have put them, are wisely put or not. But it is the study of tolerance that has raised these questions in a specially urgent form (*16, 20*), and that, in due course, will make an important contribution to the answers.

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Immunological Recognition of Self

Such recognition suggests a relationship with processes through which functional integrity is maintained

F. M. Burnet

I like to think that when Medawar and his colleagues showed that immunological tolerance could be produced experimentally, the new immunology was born. This is a science which to me has far greater potentialities, both for practical use in medicine and for the better understanding of living process, than the classical immunochemistry which it is incorporating and superseding.

In this article I shall be concerned almost exclusively with theoretical aspects of immunity. Medawar has spoken of the experimental aspects of acquired immunological tolerance and other types of immunological nonreactivity, and he has touched on the impossibility, in natural chimeras, of demonstrating that the genetically alien cells are treated in any way differently from cells that are genetically proper to the body. For me, acquired immunological tolerance means simply that the content of self-components in the body has been enlarged by an experimental manipulation. Basically, I shall deal in this article with a single problem: How does the vertebrate organism recognize self from not-self (in the immunological sense), and how did this capacity evolve?

Nature of Antigen and Antibody

The production of antibody is not the only, nor I believe the most important, manifestation of immunity, but for reasons both historical and of experimental convenience antibody is likely to remain the touchstone of immunological theory. Any formulation of theory must cover the nature of antibody and lay down the conditions under which it will or will not be produced. In this article I am concerned for obvious reasons only with antigens derived from the cells of other vertebrates and tested for antigenicity in a defined species of mammal; in experimental work rabbits and pure-line mice are the most usual, but much work on the border line between therapy and experiment has also been carried out in man.

Bovine serum albumin is antigenic in a rabbit, rabbit serum albumin is not. Both have presumably the same function in their proper species, and the difference responsible for antigenicity can be regarded genetically as an example of neutral polymorphism. Superficially at least, the differences seem to have no relevance to survival. Serum albumin is a well-defined protein, but no laboratory has yet attempted to ascertain its full chemical structure. At present there are only two proteins whose primary polypeptide structure is known, insulin and ribonuclease, and only in the case of insulin have we information as to how structure varies according to the species from which the protein is derived. Insulin is a very poor antigen—otherwise we could not use bovine insulin successfully for the treatment of diabetes. Nevertheless it *can* function as an antigen in man, and it is known that when immunological resistance to beef insulin develops, replacement by pig insulin will usually allow effective therapy.

Since Sanger's work (*1*) it has become well known that species differences between insulins involve primarily a group of three amino acid residues, numbers 8, 9, and 10, on the A chain. Human insulin differs from other mammalian types by having a different C-terminal amino acid on the B chain (*2*).

The immunological difference between beef insulin and human insulin, which is presumably responsible for the antigenicity of the former in some human beings, is thus limited to a very small portion of the whole molecule. It may be either the actual difference at positions A8, 9, and 10 or some change in the secondary structure of the molecule dependent on this difference that gives rise to the effective antigenic determinant.

This consideration of insulin as the only available antigen whose chemical structure is known leads to a conclusion which could be supported by many other pieces of evidence—that is, that an antigenic determinant has very much the quality of a gene. Its existence can only be recognized by virtue of its *difference* from something else of the same general quality. A protein or other type of macromolecule is antigenic because it carries one or more chemical configurations (antigenic determinants) which differ from any configurations of the same general quality that are present in the animal being immunized.

There is evidence which I need not particularize that an antigenic determinant, like the active patch on an antibody molecule with which it combines, is small (perhaps 100 to 200 A^3) and that to be active it must be part of an appropriate carrier macromolecule and in an accessible situation in the molecule. There is no evidence as to how many potential antigenic determinants there are in an insulin molecule. One could guess that there were some hundreds of different patterns produced by knots of three to five amino acids accessible on the surface of the molecule, any one of which might serve as an antigenic determinant, but until we know more about the requirements for antigenicity we cannot be sure that it is not a much smaller number. In practice, of course, all these potential determinants have the same structure as the corresponding substance in the immunized animal and are therefore inert.

If my last statement is correct, and I believe most immunologists would accept it, then it allows us to pose the basic problem of immunology in a spe-

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cific form. How can an immunized animal recognize the difference between an injected material like insulin or serum albumin from another species and its own corresponding substance?

Immunological Information

Clearly this is a problem of information. It is conceivable that a substance could be recognized as foreign if it were built up of chemical configurations insusceptible to enzymic breakdown by the available mechanisms of the animal involved. This may have some relevance to microorganismal antigens but not to the substances of vertebrate origin that are our present concern. Their recognition, in the sense in which we are using the word, requires that there be available in the body a large volume of accessible "information" with some superficial analogies to a dictionary. In other words, there must be something against which a configuration can be compared, and on the basis of which a decision can be made as to whether it corresponds or not. We find somewhere a combination of letters *RAXE*, and we use an English dictionary to find that there is no such word in English. If the body is to differentiate between self- and not-self configurations, the only general form of solution that has so far been thought of requires the presence of a complete set of complementary steric patterns in some accessible form which correspond to either (i) all configurations *not* present in body components, or (ii) all configurations *present* in body components, or (iii) all configurations, but in two categories corresponding to (i) and (ii).

Of these alternatives the first is obviously the most attractive, providing a *positive* recognition of any configuration against which reaction will be necessary. It is the only one which I will elaborate here; neither of the others has been seriously considered by anyone. I should agree with Jerne that the information needed may be compared to a "purged xenotypic dictionary" (*3*).

To clarify this concept we might adopt the currently popular convention of discussing "coding" problems of polypeptide synthesis by identifying amino acid residues with letters of the alphabet. If the small specifically patterned areas of an antibody molecule are constructed of a small segment or knot of a polypeptide chain, we could legitimately simplify matters by regarding all specific antibody patterns as being four-letter words—*axqb*, for example—each corresponding to an antigenic determinant represented by the upper case form of the same letters, *AXQB*. We could generate the type of information we require in the alphabetical analog by first requiring a computer to produce, say, 10^7 random four-letter combinations. The combinations are scrutinized as they are produced by a team of English speakers who eliminate every combination which forms an English four-letter word. All other combinations are stored in the computer's memory to be called into activity whenever the corresponding upper-case group is fed into the machine.

Translated into biological terms this requires some process of randomization to provide the primary array of complementary steric patterns. The elimination of self-reactive patterns would, by hypothesis, result when prenatal contact with self-components occurred. The residue would be available to react with and "recognize" foreign configurations entering during the period of independent life.

Two suggestions have been made as to the carriers of the patterns. Jerne postulated the circulating globulins, Talmage (*4*) and I (*5*) both preferred mesenchymal (lymphoid) cells. I believe that circulating globulin can be categorically eliminated in view of the phenomena of graft-versus-host reactions and that any attempt to give an observable basis to the concept must be concerned with the immunologically competent cell.

This is a term which is used differently by different immunologists. I prefer to define an immunologically competent cell as one which is specifically stimulated to some reaction (either observable or in principle observable) by contact with an appropriate antigenic determinant. In order to illustrate this concept of the immunologically competent cell, I shall make a brief diversion from theory to experiment. For the last three years we have been interested in the graft-versus-host reaction that is shown when normal fowl leucocytes are inoculated onto the chorioallantoic membrane of chick embryos. Figure 1 shows four membranes, all from eggs laid by a single hen and fertilized by artificial insemination from the same cock. Both birds are from the same highly inbred strain of White Leghorns.

On each membrane we inoculated about 2×10^6 leucocytes from the cock and reincubated the embryos for another 4 days. As harvested, two of the membranes show no lesions; the others show between 100 and 200, with marked opaque foci about 1 millimeter across. These lesions mark areas of cellular proliferation in which both the embryonic (host) cells and the mature (donor) cells and their descendants play a part. The foci represent an immunological response initiated by individual immunologically competent cells; antibody production is not involved. We believe that the difference between positive and negative membranes is due to the presence of a single antigenic determinant in the embryos showing lesions and to its absence in the embryos that show none (*6*). There are several interesting features about these foci: (i) they are immunological in character; (ii) they are produced by *normal* lymphocytes from completely normal birds; (iii) each lesion is almost certainly induced by a single cell, but only about one lymphocyte in 10^4 can induce lesions; (iv) the lesion is initiated either immediately or within a few hours of depositing the cells on the membrane.

There could hardly be a more direct demonstration of the potentiality of the immunologically competent cell, and although with sufficient ingenuity the facts can be pressed into the mold of an instructive theory, they fulfill naturally and easily the requirements of a theory calling for cellular carriage of previously generated information that will allow recognition of a given antigenic determinant.

At the present time I believe there is very little doubt among immunologists that some form of selective theory of this general form is needed. The whole domain of homograft immunity and tolerance, graft-versus-host reactions, and histocompatibility genes demands a cellular basis of immunity and a "selective" rather than an "instructive" origin of immunological specificity.

By adopting the idea of randomization of pattern we imply that during embryonic life a very large range of patterns is synthesized in such a fashion that in later life any one of the patterns can be produced in large numbers on demand. If the patterns are carried eventually in lymphoid cells, we must presumably look for some process of differentiation or somatic mutation in the primitive cells ancestral to the lymphoid series. Most geneticists and

immunologists would probably prefer to look for randomization of pattern in a hypermutability of one or more genetic loci at some stage during embryonic life, with a relative stabilization subsequently. This is in line with the general dogma that the pattern of a protein is determined in the last analysis by the pattern of a segment of chromosomal deoxyribonucleic acid.

In this way we can picture clones of cells arising which carry the capacity to synthesize, under appropriate stimulus, one, two, or more specific patterns which, either as a cell receptor or as the active patch on an antibody molecule, could react each with a specific antigenic determinant.

There are two ways at least in which the functional elimination of patterns reactive with self-components could be implemented. If a cell or clone is limited to one or two patterns, then it is practical to postulate that any clone carrying either one or two self-reactive patterns is eliminated, leaving only clones carrying patterns corresponding to configurations not present in the body. This is the form taken by the clonal selection theory, and provided two is adopted as the usual number of patterns for a diploid somatic cell, it provides a reasonable interpretation of the facts.

As both Lederberg (*7*) and Monod (*8*) have pointed out, there is no special reason why only two patterns should be produced by a process of hypermutation. It is obvious, however, that any increase above two will make it progressively more difficult to sort out patterns corresponding to self- from those corresponding to not-self configurations by elimination of clones. If there are 10 or 20 random patterns per clone, the elimination of reactivity against self-configurations must be accomplished by some process of inhibition that still leaves potential activity with those patterns which are complementary to foreign antigenic determinants.

Many immunologists are impressed with the fact that, in general, tolerance induced in the perinatal period only persists when the antigen in question remains present in the body. They feel that this points to an inhibitory or blocking action rather than the elimination of the cells concerned.

It is not difficult, in fact, to picture an inhibitory process of the type needed, but to do so requires a little preliminary discussion. The difference between a primary and a secondary immune response is known to everyone who has ever been concerned with practical immunization procedures. Modern work suggests that there are several levels of physiological reactivity that can be manifested by a clone of immunologically competent cells. At least three, which we can call grades 0, 1, and 2, are probably necessary, grades 1 and 2 corresponding to the cells responsible for immune responses of primary and secondary type, respectively.

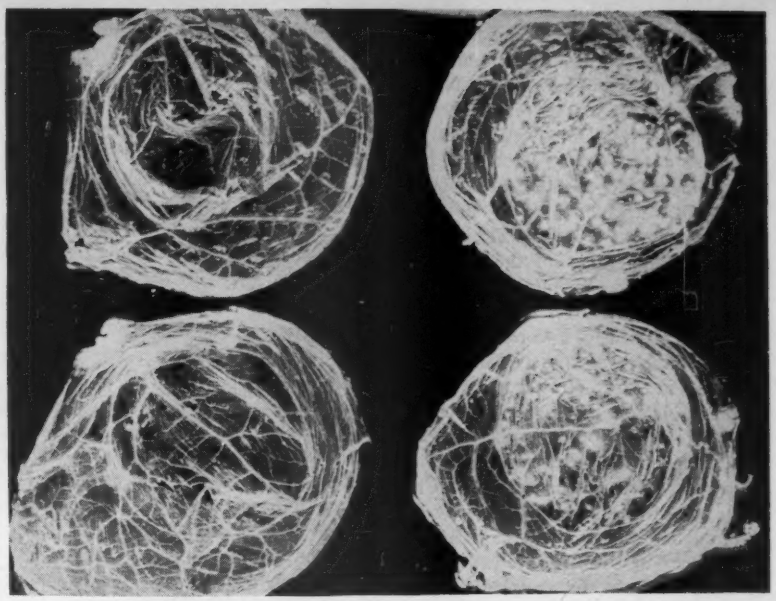

Fig. 1. Typical graft-versus-host foci on the chorioallantoic membrane. Leucocytes from a cock of an inbred strain were placed on four membranes, each from an egg laid by a hen of the same inbred line and fertilized by the donor cock. Note the segregation for the factor, which allows the appearance of foci.

In grade 0, characteristically but not exclusively present in embryonic life, the only reactivity that need be postulated is an inhibition of part or all of the cellular activity by contact with the antigenic determinant. One assumes that, after birth, initial contact of antigen with a grade 0 cell gives rise to grade 1, perhaps directly, perhaps by way of proliferation. In grade 1 we have cells capable of specific proliferation after contact with antigenic determinant and capable also of producing reactions of delayed-hypersensitivity type. For antibody production, grade 2 cells must be produced, presumably by antigenic stimulation of grade 1 cells. The essential lesion in agammaglobulinemia is a failure of the change from grade 1 to grade 2 to occur.

Any cellular theory of immunity demands the presence of cell receptors which, by making an antibody-like union with antigenic determinant, can provoke reaction of one sort or another. The difference between the grades of reactivity could well depend on the number and accessibility of these receptors. In grade 0 in the embryonic phase or its equivalent, the receptors are few and, perhaps because of their situation, are readily blocked for a prolonged period by molecules carrying the antigenic determinant. This appears to be the type of reaction that Smith (*9*) favors as an explanation of his experiments on acquired tolerance in rabbits. If all cells carrying the embryonic grade 0 receptors for antigen X have all these receptors blocked so that they can neither react with any further antigen nor mature to a higher grade, this would provide as adequate an explanation of tolerance as elimination of the clones concerned. A qualifying hypothesis would probably have to be added, to the effect that when a receptor was released by metabolic breakdown of the antigenic determinant, it would remain in the nonreactive phase long enough for it to be found and again inhibited by other molecules of the blocking antigenic determinant.

Given sufficient time (perhaps a few days) free from antigen, a receptor would presumably mature to grade 1 and behave like normal unstimulated receptors. Once grade 1 is reached,

specific contact with a receptor becomes a stimulus to proliferation and perhaps, in special environments, to plasma-cell development and antibody production.

Such a concept can be represented in diagrammatic form for a cell (or clone) assumed to have two patterns corresponding to self-components 1 and 2 and two corresponding to non-self patterns *a* and *b* (Fig. 2). The advantages of a hypothesis of this sort are that it (i) provides a simpler interpretation of the necessity for the continuing presence of antigen if tolerance is to be maintained indefinitely, and (ii) allows the existence of a complete range of immunological patterns with a much smaller number of clones than would be required if every clone carrying a self-pattern had to be annihilated. Unfortunately from the point of view of experimental test, a hypothesis in which the number of patterns available to a clone is, or may be, large soon becomes experimentally indistinguishable from an instructive-theory hypothesis.

I am concerned with immunological theory primarily only in so far as it deals with the problem of self-recognition. It is obvious, however, that any theoretical formulation must also be acceptable as an interpretation of the other significant aspects of immunity. A brief reference should therefore be made to the possibility, which cannot be altogether excluded, that genetic information can be transferred from one somatic cell to another, by some process analogous to processes known to operate in bacteria. If, after a primary elimination of self-reactivity along one or other of the lines described, antibody-producing capacities could be transferred from one clone to another, this would have some obvious advantages in relation to immunological memory.

To summarize this discussion of the basis of self-recognition and tolerance, I have given reasons for believing that the only possible type of approach is by a "selective" theory of immunity which must be developed on a cellular, and probably on a clonal, basis. Within these limitations there are several possible alternatives in regard to the number of potential patterns carried by a single cell or clone and the means by which patterns complementary to body components can be inhibited or eliminated.

This is not the place to elaborate other aspects of immunological theory, nor would I have any novelty to offer if I did so. It is only in relation to the first stage of the immune process—the recognition of foreignness with its implication of pre-adapted patterns—that there is serious controversy. Once the immunological competence of a cell has been unmasked (according to selectivity theory) or produced by antigen (according to instructive theory), the interpretation of phenomena arising subsequently, including antibody production and immunological memory, hardly differs from one theory to the other.

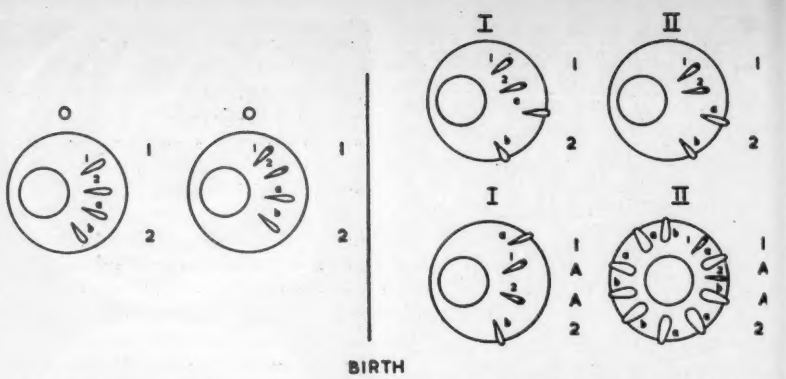

Fig. 2. Diagram indicating the possible validity of a clonal-selection hypothesis, with fairly numerous potentialities per cell. (1, 2) "Self"-type antigenic determinants and the corresponding reactive units in the cell. (*A*, *B*) Foreign antigenic determinants; (*a*, *b*) the corresponding cellular units. The changes on exposure to the antigenic determinants shown outside the cells are described in the text.

Evolution of the Immune Process

To anyone with a speculative turn of mind there are very interesting problems in the evolutionary origin of the processes we have been considering. It is not difficult to persuade oneself that the development of immunity against pathogenic microorganisms is of survival value, but for many years I have found this a rather unsatisfying and naive approach. The phenomena of tolerance and of the nonantigenicity of self-components seem to be more basic than those of postinfectious immunity. I cannot conceive that they evolved from an earlier process concerned only with protection against recurrent infection, whereas I *can* conceive that the converse took place.

The question then becomes, Why and how, in the evolutionary sense, did warmblooded vertebrates develop the capacity to recognize the presence of foreign configurations in the body and to initiate a process of eliminating any cells so recognized?

There are several possible lines of thought here, but the only one I find attractive concerns the significance of somatic mutation in metazoan organisms, particularly in complex, large, and long-lived vertebrates.

It is axiomatic that mutation supplies the raw material for evolution. In other words, the whole evolutionary process depends on the possibility of error in replication that is necessarily associated with mitotic division. This possibility of error must be at least equally present in the replication of somatic cells. One of the requirements, therefore, for the success of a large multicellular animal is that any potentially dangerous mutations in proliferating somatic cells should be eliminated before they can cause serious damage in the evolutionary sense. The most serious effect that could be due to a somatic mutation or series of mutations is, of course, malignancy, but there are other possibilities as well which might have undesirable effects in special situations.

According to present-day thinking, every mutation must result in the appearance of a protein of pattern different in some respect from a normal protein. This follows simply from the absence of any known way in which a change in nucleic acid structure can influence phenotype except via a protein, usually pictured as an enzyme. The existence of immunological changes or deletions in somatic mutant (malignant) cells has been described on many occasions, and there is evidence of serological and cellular immunological responses to some spontaneous tumors. There could well be survival advantage in being able to recognize the presence of cells carrying wrong molecular con-

figurations and to eliminate them from further proliferation. It would profit the organism to maintain a surveillance over the orthodoxy of its chemical structure and to stamp out heresy before it could spread. To be able to do this would require just such a mechanism as is called for by the facts of immune tolerance. On this view, the faculty of immunological recognition becomes an intrinsic part of the homeostatic controls that maintain the body as a going concern. And once in existence, it could clearly provide the basis for the development of anti-infectious immunity.

To provide an evolutionary interpretation of a physiological process, however, requires something more than the demonstration that it has survival value to the possessor. We must also offer some hint as to how it might have developed from pre-existent faculties. Here there is an obvious suggestion that immunological recognition is an inevitable derivative of the basic requirement for any integrally organized, multicellular organism—the existence of an elaborate system of information and control, of receptor, effector, and feedback mechanisms, that is needed to maintain morphological and functional relationship between cells. Some of this—perhaps a large proportion—must be mediated, as Paul Weiss has suggested, by complementary pattern relationships between macromolecular constituents. This may seem to be a very thin speculation which could not possibly stimulate a line of experimental inquiry. It may be foolish to attempt to interpret immunity in terms of processes like differentiation and morphogenesis that we know extremely little about, but the converse possibility, that light might be thrown on differentiation from work in the more experimentally amenable field of immunity, is too inviting to be neglected. There has been a recent suggestion, moreover, at the experimental level which seems to point in just this direction.

During the last few months I have been deeply interested in an obscure organ of the chick embryo. The bursa of Fabricius is a diverticulum from the hind-gut which develops a complex of folds covered with entodermal epithelium and containing loose mesodermal cells and frequent regions of hemopoietic tissue. About the 14th to 16th day of incubation, nodules of rapidly growing epithelium develop and expand into the mesodermal tissue. According to Ackerman and Knouff (*10*) (and all our own observations are in accord), these epithelial cells begin to lose their epithelial packing, and about the 18th or 19th day, the center of the nodule becomes indistinguishable from a germinal center of lymphoid tissue. Subsequently, a lymphoid structure somewhat analogous to the thymus develops and appears to play an important part in antibody production in the chicken. Like the thymus, it reaches a maximum when the chicken is about 4 months of age and thereafter atrophies. When we take into account the epithelial origin of the thymus, we have a shadow of justification for wondering whether the antibody-producing system, the immunologically competent cells, may not have been derived, phylogenetically and ontogenetically, from cells which had once had, as it were, morphological responsibilities. The immunological significance of the thymus and the bursa of Fabricius is one of our present main areas of investigation.

Conclusion

My part in the discovery of acquired immunological tolerance was a very minor one—it was the formulation of a hypothesis that called for experiment. The clinical and experimental facts that have been recognized since Medawar and his colleagues opened the way have emphasized again and again the importance of self-recognition in immunology. This, I believe, is something which in its turn calls for new hypotheses. In this article I have tried to present as briefly as is consistent with reasonable clarity my thoughts about the theoretical implications of immunological tolerance and self-recognition. The hypotheses that have been stated are modifications of earlier hypotheses, modifications enforced by the advance of experiment and observation. I have only at two points introduced new factual material, and I have done this to illustrate that the approach being used is not meaningless speculation but suggests experiments that may lead to its modification or rejection.

I have introduced ideas about the evolution of the process of self-recognition because, as a biologist, I believe we know less about the processes of differentiation and morphogenesis than about any other major field in biology. There is an insistent suggestion that immunological self-recognition is derived from the processes by which morphological and functional integrity is maintained in large and long-lived multicellular organisms. This may be a mere cobweb of phantasy, but in my more optimistic moments I can hope that it may also function like Ariadne's thread to guide us effectively through part of that biological labyrinth, the process of differentiation.

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Limitations on Space Flight due to Cosmic Radiations

Newly discovered radiations dictate vehicle design and orbit of future manned space flights.

Howard J. Curtis

One of the factors which may severely limit man's operation in space is the presence there of various ionizing radiations. Until very recent years the possibility of putting men in outer space seemed so remote, and the radiations there appeared so weak, that the problem was largely ignored. However, with the development of rocket systems capable of placing satellites in orbit around the earth and with the prospect of placing manned satellites in orbit in the near future, the problem of radiation hazard is both a real and an immediate one.

Cosmic rays have been known and studied for many years. Mainly originating outside the solar system, they consist of atomic nuclei accelerated to very high velocities (*1*). They are present in the vicinity of the earth only in very small numbers and until very recently have been of only theoretical interest to biologists.

When the first American satellite (1958 Alpha, Explorer I) went into orbit on 31 January 1958, there were instruments aboard which gave an indication of a very high radiation field outside the earth's atmosphere; this finding was definitely confirmed when the next satellite was placed in orbit. It was soon found that the radiations involved were quite different from the cosmic rays, and it appeared that the intensities were great enough to be a real hazard for manned space vehicles.

Thus an interest was created in these radiations and the effect they might have on a man in space. Since the newly discovered radiations differ so completely from cosmic rays, in both physical and biological aspects, it will be best to discuss them separately.

Van Allen Radiation Belts

Since their discovery these radiations have been very intensively studied. Within a year it was found that the radiations consist almost entirely of electrons and protons and are confined largely to two zones surrounding the earth, with maximum concentrations occurring in the plane of the magnetic equator; the peak intensity in each zone occurs roughly at 3500 and 18,000 kilometers from the surface of the earth (Fig. 1). They are usually referred to as the Van Allen radiation belts, after their discoverer.

Present theories of these radiation belts postulate that the particles are trapped by the earth's magnetic field and may remain there for considerable periods of time. As an electron or proton travels toward the earth from the sun, it encounters the earth's magnetic field, which deflects the particle toward either the north or south polar regions in such a way that it spirals around a line of force. As the particle approaches the earth, the converging magnetic lines of force cause it to be reflected back along the same line toward the opposite pole, where the process is repeated. Thus, the particles may continue their back-and-forth motion for days or perhaps months, even though a single traverse may take only a few seconds or less.

Although the origin of charged particles in the radiation belts has not been fully established, it appears that most, if not all, are of solar origin. One hypothesis (*2*) assumes that the particles of the two belts have different origins. According to this hypothesis, those of the outer belt originate in the sun, perhaps as a result of a solar eruption, and after being trapped in the geomagnetic field are lost slowly by collision with the very sparse atmosphere. They are then replenished at the next time of solar activity. In times of violent solar activity the particles "spill over" in large numbers in the upper atmosphere in the polar regions, thus accounting for the aurorae.

According to this theory, many of the particles of the inner belt have a different origin. Primary cosmic ray particles, traveling at too high a velocity to be trapped by the earth's magnetic field, are stopped in the high atmosphere partly by nuclear collisions which lead to nuclear disintegrations, producing neutrons which radiate in all directions. As neutrons are unstable and decay spontaneously into electrons and protons, those neutrons which travel away from the earth can provide a source of charged particles which are then trapped in the magnetic field and produce the inner Van Allen belt.

This theory is very attractive and thus far is supported by satellite and space probe observations. It is known that the radiation in the belts varies greatly with solar activity, and the position of the belts probably varies considerably as a function of time.

Thus, outside the earth's atmosphere there is a radiation field which continually waxes and wanes and shifts about very considerably. Some average values have been estimated by Van Allen (*3*), and these are given in Table 1; they can be taken at the present time only as rough approximations.

So far these radiation belts have not been found at an altitude of less than 600 kilometers; it seems reasonable to assume that this represents an approximate lower limit for the inner belt and that no great hazard to man will be encountered below this altitude.

Assuming the values of Table 1 to be correct, one can compute the biological dose under any desired condition. First, if one assumes a condition of no shielding it is possible to predict a dose of radiation of millions of rads per hour at the peak intensity of both radiation belts. (A rad represents a dose of radiation received when 100 ergs of energy per gram of matter has been absorbed.) It should be noted that a dose of 500 rads is probably fatal to man; 100 rads would cause serious later effects; and 10 rads would cause

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only minor effects. These figures mean that it would be impossible for man to exist in the radiation belts unshielded, even for very short periods of time.

The slight protection offered by a space suit would cause some change in the situation, but the dose rates would still be thousands of rads per hour. This means that if man is required to operate in space at an altitude of, say, 10,000 miles in the neighborhood of the equator, he would receive a fatal dose of radiation in a few moments. If he were in a space vehicle with shielding thick enough to provide a mass of 1.0 gram per square centimeter of surface area (a reasonable shell for a space ship), the situation would change considerably. The dose rate would be about 10 rads per hour in the inner zone and 50 rads per hour in the outer zone; thus a traverse, lasting some minutes, of one or both of these belts in such a ship would be admissible, but repeated exposures could not be tolerated.

It should be emphasized that Van Allen's values may be in error by an order of magnitude. For example, Schaefer (*5*), computing from some data of Freden and White (*6*), concludes that the maximum dose rate in the inner belt behind shielding of 2 grams per square centimeter would be about 120 rads per hour, as opposed to 10 rads per hour behind shielding of 1.0 gram per square centimeter, as estimated from Van Allen's data. Nevertheless, it seems reasonable to assume that shielding of 10 grams per square centimeter would be required to shield against virtually all the radiation of the outer belt. This would be a heavy but perhaps not impossible load. In the inner belt there is a strong component of very energetic protons, and a much heavier shield would be required. However, the flux of these particles is not great, so a brief stay in this zone with a moderately heavy shield would probably not be serious.

From these estimates it can be seen that a satellite having an orbit which passed through even the fringes of the radiation belts would be habitable for only an hour or two. For a rocket which leaves the earth, the escape velocity is such that, with reasonably heavy shielding, a man would receive a dose of the order of 10 rads. The "escape hatch" at the poles could be used, but this route is much more difficult technically.

In the foregoing discussion, it is assumed that all radiations have the same biological effect. This is not strictly true. The relative biological effectiveness of protons of about 1 Mev energy is about 2.3 as compared with gamma rays, but when the energy increases to about 20 Mev, the relative biological effectiveness approaches unity. The radiations which would be encountered inside a space ship passing through the Van Allen radiation belts would have all the slow components filtered out by the walls of the ship; only fast electrons, fast protons, and some x-rays would be left. These all have roughly the same relative biological effectiveness, and thus the correction required by this factor would seem to be minor.

X-rays will be generated when the electrons of the radiation belts are stopped in the walls of the space ship (bremsstrahlung). The magnitude of these x-rays will depend not only on the weight of the shield but also on its composition and design. The correct design of a shield for a complex radiation spectrum such as exists in the radiation belts is a difficult mathematical problem. However, with careful shield design such x-radiation can probably be kept to reasonably low values and, for any situation likely to be encountered in a space ship, will probably always be well below the radiation doses received from particles which penetrate the shield.

Recent measurements (*4*) have shown the presence of x-rays of energies up to 90 kev as a normal component of solar radiation, but these do not, of course, penetrate the earth's atmosphere very far. These measurements have shown that most of this radiation is in the very soft x-ray region below 10 kev, and penetration through a shield satisfactory for protection from other radiations would be so slight as to be negligible. In the harder x-ray region (30 to 90 kev), the flux is so low that it can be ignored as a biological hazard.

Thus, it would seem that the Van Allen radiation belts present a challenging problem to those interested in putting a man in space. There is every

Table 1. Energy spectrum of radiations in the radiation bands. [From Van Allen and Frank (*3*)]

Particles	Energy	Intensity
	Inner band	
Electrons	> 20 kev, unidirectional	2×10^9/cm² sec sterad
Electrons	> 600 kev, unidirectional	1×10^7/cm² sec sterad
Protons	> 40 Mev, omnidirectional	2×10^4/cm² sec
	Outer band	
Electrons	> 20 kev, omnidirectional	10^{11}/cm² sec
Electrons	> 200 kev, omnidirectional	10^8/cm² sec
Protons	> 60 Mev, omnidirectional	10^2/cm² sec

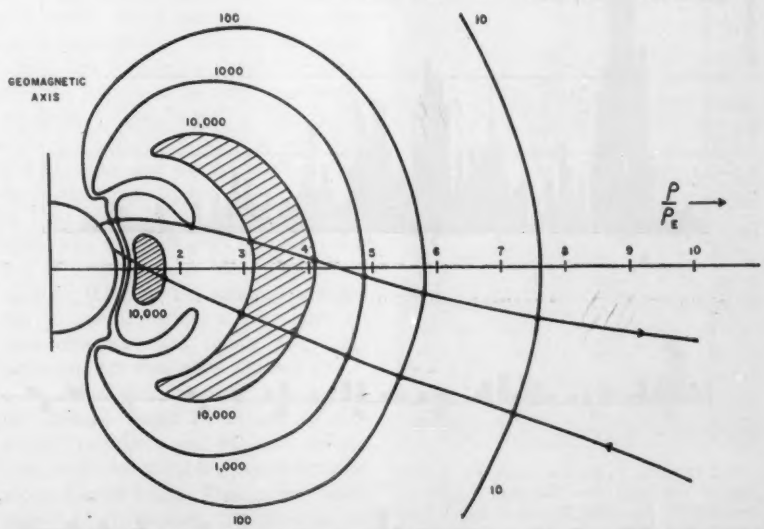

Fig. 1. A plot in a geomagnetic meridian plane of the intensity of the radiation belts around the earth. The contour numbers represent the counting rates recorded from a Geiger-Muller tube in Pioneer III or in satellite 1958E. The cross-hatched areas represent regions where the counting rate may be much higher than 10,000. [From Van Allen and Frank (*3*)]

indication at the present time that with careful planning these problems can be solved, so that radiation hazard will be no greater than the many other hazards associated with space flight.

Effects of Cosmic Rays

Primary cosmic rays consist of charged atomic nuclei, stripped of their planetary electrons; atomic nuclei of all the elements in the periodic chart up to iron have been observed in these radiations, although not all in equal numbers. They apparently originate outside the solar system and pervade the galaxy. The earth's magnetic field imposes an energy cutoff condition such that the cosmic ray flux is greater near the magnetic poles and at a minimum in the plane of the magnetic equator. The nuclei interact with the earth's atmosphere, and the heavy particles do not penetrate below an altitude of about 16 kilometers, terminating in nuclear reactions in the upper atmosphere.

These radiations can be divided into two parts—the lighter group, consisting of protons and helium, on the one hand, and all the heavier elements on the other. The former group has a much higher flux; it has been estimated that there are about 50,000 particles in this group per square centimeter per day striking the earth's atmosphere, as compared to about 500 of the heavy group (Fig. 2). The heavy group contributes more ionization in the high atmosphere per particle, but the lighter particles contribute most (perhaps ten times as much) to the total ionization produced. From these figures one can estimate that a man in an unshielded situation at an altitude of 100,000 feet or more would receive a total radiation dose of the order of 15 millirads per day. Since such a dose is due almost entirely to protons, of which the biological effects are well known, one would be inclined to neglect it as being too small to be of any importance in human space travel. However, there has been some recent evidence indicating that the heavy particles, even though producing a relatively negligible amount of ionization (dose), may produce special biological effects of considerable importance. It thus becomes necessary to examine these effects critically.

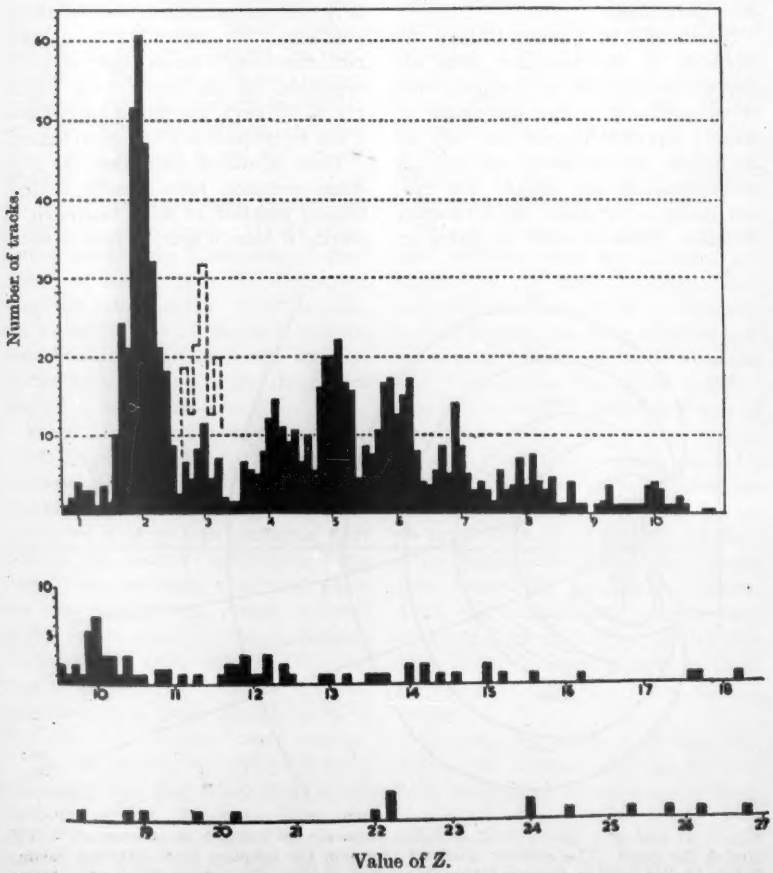

Fig. 2. Distribution of primary cosmic ray particles as a function of atomic number. The tracks from very heavy particles are quite rare events. [From Dainton *et al.* (*11*)]

The primary cosmic rays may have energies as high as 10^{7} Bev per nucleon, but particles with such high energies are extremely rare, and most of the particles have energies of a few billion electron volts per nucleon. When they enter tissue one of two things may happen. First, they can interact with the atomic nuclei in the tissue to form stars. In this process the particle makes a head-on collision with an atomic nucleus of the tissue, resulting in nuclear disintegration from which a number of small high energy particles and some gamma rays are emitted. Since these secondary radiations are very penetrating, the energy of the primary radiation is dissipated over a large volume of tissue and is of relatively small radiobiological importance.

The second possibility is that the primary particle may gradually lose its energy by collisions with the electrons of the tissue. Not only does this process cause ionization of the atom of the electron in question but the electron itself is ejected at an angle to the track of the primary particle and causes additional ionization close to this track. This dual process causes intense ionization along the particle track. As the primary particle slows down, its rate of energy loss becomes larger and larger, so that toward the end of the particle path the track of ionization becomes quite wide and intense (Fig. 3). Schaefer (*7*) has calculated the energy distribution in these tracks under a variety of conditions. Briefly, he computes that the area of intense ionization occurs only at the end of the track and is only about 1 millimeter long, even though the particle may penetrate many centimeters of tissue. This intense effect is known as a "thin-down," which can be as wide as 25 microns. In the center, the ionization density is equivalent to doses of the order of 10,000 rads, with the dose decreasing radially from the center. Thus, a thin-down would produce a small cylindrical volume of intense ionization about 1 millimeter long and up to 25 microns in diameter. A maximum of 15,000

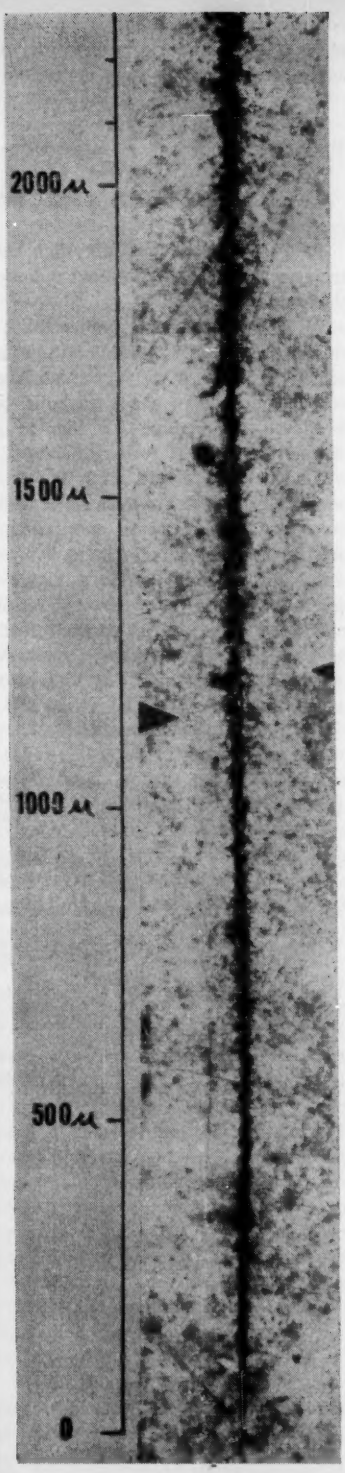

Fig. 3. Track of a heavy cosmic ray primary of atomic number about $Z = 20$ in a photographic emulsion. The emulsion has a density of about 3, so the spread of the track would be much wider in tissue. [Modified from Schaefer]

mammalian cells would be involved in such a volume. Schaefer has further estimated that a man weighing 70 kilograms would receive about 100 such hits per hour in interstellar space. Since most of the cells involved would receive only a relatively small dose and would therefore be unaffected, thin-downs would seem to constitute only a minor hazard except for certain organs where the loss of a relatively few cells would be very serious. The organs most likely to be affected would be the hypothalamus of the brain or the lens of the eye. In the former case, small brain nuclei are responsible for such functions as temperature regulation and, in the latter, a small defect may grow to form a cataract.

These thin-downs represent quite a different type of radiobiological action, on which there has been little laboratory experimentation. The energies of these particles are greater than 1 Bev per nucleon, while the best of the heavy ion accelerators, the HILAC at Berkeley, can accelerate ions to only 10 Mev per nucleon. Single cell organisms such as yeast are being studied with the HILAC, but the lower energies involved may not produce significant changes in terms of tissue damage.

An attempt has been made by Chase (*8*) to measure directly the biological effect of these thin-downs by sending black mice in balloons to the top of the atmosphere at altitudes up to 120,000 feet. It was observed that some of these black mice grew some gray hairs. Hairs turn gray when the melanin-producing cells of the individual hair follicle are destroyed; these cells are known to be very sensitive to radiation. Thus, when a hair turns gray in a young mouse, it is presumptive evidence that the follicle has been hit by radiation. In one series of studies in 1954, involving three balloon flights, there was a significantly greater number of gray hairs on the experimental animals than on the control animals, but in another series a year later no such difference was found. These experiments are thus quite inconclusive.

In these thin-downs practically all the damage would be caused by secondary radiation, and the only unique feature would be its high concentration along discrete paths. Thus, a very small beam of radiation, 25 microns in diameter or less, should produce the same effect in tissue as a single primary particle. Such a microbeam has been developed, and experiments have been undertaken by Zeman, Curtis, Gebhard, and Haymaker (*9*) in which they used the brain of a mouse as the experimental tissue. The microbeam consists of deuterons from the 60-inch Brookhaven cyclotron collimated in a beam whose diameter can be varied from 25 microns to 1 millimeter. It is found that with the large-beam diameter a dose of 14,000 rads will cause almost complete destruction of cells of the cerebral cortex along the beam path, as judged by histological examination. This result is to be expected from experience with x-ray. However, as the beam diameter is decreased, an increasingly large dose in the beam is required to cause cell destruction, until at a beam diameter of 25 microns, more than 400,000 rads is required (Fig. 4). This is a very striking phenomenon.

These results can most easily be explained by assuming that with a wide

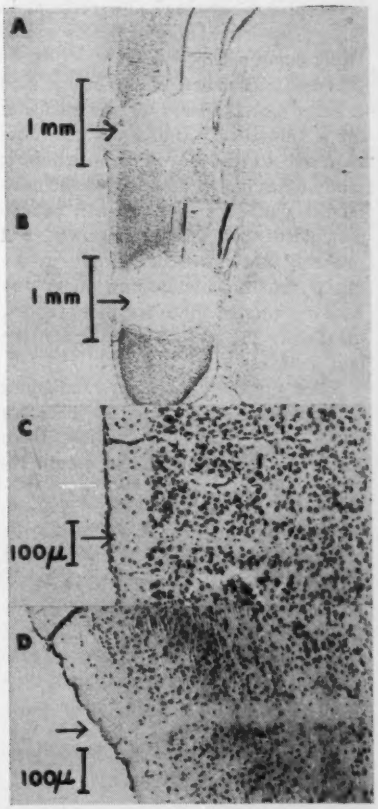

Fig. 4. Frontal sections of cerebral cortex of mice irradiated with deuteron beams: (*A*) 1-mm beam, 50,000 rad, 24-day survival; (*B*) 1-mm beam, 60,000 rad, 24-day survival; (*C*) 0.025-mm beam, 1.1×10^5 rad, 6-day survival; (*D*) 0.025-mm beam, 1.1×10^6 rad, 48-day survival. [From Zeman *et al.* (*9*)]

radiation beam most of the effect seen in the brain is secondary to vascular damage. As the beam becomes very narrow it has an excellent chance of going through the tissue without hitting even one capillary, since the average distance between capillaries in the brain is 65 microns. Even if the beam did hit and destroy a single capillary, it seems certain that other, neighboring capillaries could carry out its function, since there must be that much of a factor of safety for the capillary circulation. It seems almost incredible that individual nerve cells in the brain can sustain a direct hit with a dose of 400,000 rads before being destroyed, but such is the case. It should be pointed out that these cells never undergo cell division, and this undoubtedly accounts for their radioresistance. In these experiments the histological appearance of the cells was taken as the sole criterion of effect. However, if a cell appears cytologically perfect 48 days after irradiation, it seems highly likely that it is functional.

Since the smallest of the beams used is large as compared to the diameter of a thin-down, and since the dose required to cause cell destruction is many times higher than that in the most intense part of a thin-down, it can be concluded that these thin-downs will probably not prove destructive to the brain. Experiments are now under way with the microbeam to test other tissues, principally the lens of the eye and the hair follicles.

Since primary cosmic radiations which will be encountered in space are so energetic, shielding against them would be very difficult and would require about 100 grams of aluminum per square centimeter of surface area to decrease their intensity significantly. Less shielding than this might make the situation worse, since it would only slow down the particles and insure that the thin-down occurred in the body.

It is worth noting that a few rockets for which recovery was planned carried biological test objects. The principal radiobiological objective was the test of the foregoing conclusions, to make sure that nothing had been overlooked. Three different types of objects have been flown: mammals, including two monkeys and some mice; microorganisms (in an attempt to observe some abnormal types of mutations); and seeds (the plant embryo constitutes a sensitive radiobiological indicator, since a change in even one cell may show up as an abnormal plant when grown). None of these experiments demonstrated any radiobiological damage—a finding which is not surprising in view of the relatively low altitude and short duration of the flight. Some biopacks have been included in satellites designed for recovery, but none has been recovered yet.

Thus it seems that at the present time the heavy cosmic ray primaries do not constitute as serious a hazard as was once feared. The actual radiation dose delivered by them is negligible, and apparently the damage to the brain would not be appreciable. The effect on the eye is not known yet, but it does not seem likely that it will prove to be a serious problem. It should be pointed out that the results of Chase on the graying of hair at a very high altitude have never been either explained or confirmed, and until this matter is settled one cannot speak with full assurance.

Summary

These conclusions (*10*) may be summarized as follows:

1) Flight below the Van Allen belts seems reasonably safe without radiation shielding.

2) It is probably impractical to shield a rocket sufficiently to permit a man to remain in the inner Van Allen belt for more than about an hour, but it should be possible for him to go through it without serious harm.

3) Shielding for the outer Van Allen belt is possible but would have to be quite heavy if a stay of more than a few hours were contemplated.

4) The primary cosmic radiation is not intense enough to deliver a serious radiation dose, even for exposures of a few weeks, and the heavy cosmic ray primaries do not seem to present an unusual hazard.

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Science in the News

A Few Headaches: Priorities for Science; Preparing for the Test Ban Talks; the Rules Committee

The National Aeronautics and Space Administration has been talking up its plans to shoot a chimpanzee on a brief voyage into space, to be followed, hopefully, within two months by a man in space for an equally brief voyage. This will not involve putting either into orbit; man and beast would be fired off like an intercontinental missile and recovered from the ocean a few minutes later.

This imminent preliminary to the Project Mercury man-in-orbit flight, the latter to follow in about another year, is being watched with great interest, but with less than great enthusiasm, by the President's Science Advisory Committee, which has for some time been convinced, or nearly convinced, that the project is costing more money than it is worth.

The cost, in this sense, is not being measured so much in terms of dollars as in terms of priorities. As the most recent published report of the committee made clear [(*Science* **132**, 1802 (16 Dec. 1960)] the advisers see a need for a number of important changes in federal policies for supporting science, almost all of which will cost a good deal of money, and all of which the committee feels are very important even though none of them have the popular appeal of what George Kistiakowsky, the retired chairman of the committee, liked to call "technological spectaculars."

What apparently worries the committee is that such spectaculars may be drawing an undue amount of support away from a more rational science program, concentrating it instead on things which have to be justified as much for their propaganda value as for their scientific value. The argument being made is not so much that the Mercury project is a waste of money: everyone agrees that man will go into space eventually, and that the money will have to be spent sooner or later. The question is how fast a project like Mercury should be pushed when excellent cases can be made for alternative sets of priorities that would give the man-in-orbit a less immediate target date and put more of the money available today into other projects.

Even on propaganda grounds the case for a near-crash program to put a man in orbit has been made to look doubtful. The new chairman of the Advisory Committee, Jerome Wiesner, was chairman of a Kennedy task force on space that questioned the emphasis on Project Mercury on the grounds that with the situation as it is the Russians are likely to beat us in putting a man in space no matter what we do. Aside from this rather weighty limitation, the propaganda value of the whole space effort will, in the long view, depend on which nation is able to demonstrate its superiority over a period of years, rather than on which is first with a particular spectacular achievement in the early 1960's. From this point of view it becomes doubtful whether rushing to be a close second to the Russians in putting a man into orbit is nearly as important as a more balanced program that, hopefully, would put us well ahead of the Russians a few years from now.

In a related case, such considerations have caused the project for building an atomic airplane to be reoriented in recent years toward spending more of the funds earmarked for this project on basic research and much less on getting an atomic airplane off the ground in the shortest possible time, despite a considerable amount of Congressional pressure to get a plane off the ground. The greatest criticism of the old Administration's failure to put a satellite in orbit before the Russians did is not that it failed to mount an immensely expensive crash program to achieve this, but that it happened to have a rocket to do the job, and for reasons that seemed good enough at the time chose not to go ahead. The point of this sort of assessment is that even in terms of astounding the world more is likely to be accomplished by relying on a well-balanced program of research to produce the spectacular results that have always come from research in the past than by pouring an immense amount of money into a particular thing that can be visualized at the moment. What is beyond the horizon will almost certainly be much better; but of course it *is* beyond the horizon. The problem for the Administration is the not easy one of working up a little more enthusiasm among Congress and the public for what is beyond the horizon.

Problem of Priorities

Putting into perspective the pressure to produce some particular spectacular is not the end of the new Administration's problems of priorities. It is barely the beginning. For the estimates of what it would cost to finance all the sound research programs that are proposed come to an immense amount of money, more than can realistically be proposed for spending. The Science Advisory Committee is trying to come up with a schedule of what should be supported, or, stated in terms that better emphasize the difficulty of the problem, of what clearly valuable projects should not be supported.

The President will then be handed the equally difficult political problem of getting the executive agencies, industrial and university forces, and Congress to go along with something fairly close to what his scientific advisers, inside and outside the Advisory Committee, have been able to convince him is a sound system of priorities. It would be much easier for him if his science advisers could only come up with a recommendation for an extra hundred million or so for research on cancer and heart disease instead of for oceanography, but things are not likely to be that convenient.

Preparing for the Test Ban Talks

The annual report of the Atomic Energy Commission, released this week, devoted a comparatively small but prominently placed part of the report to a warning on the dangers of continuing the current unpoliced moratorium on underground weapon testing. As had doubtless been intended, this was the portion of the report that

made headlines. It made the point, which no one in a position of responsibility denies, that the current de facto, unpoliced ban cannot be allowed to continue indefinitely. It implied what is in dispute: that the unpoliced ban has already run so long that the need for putting an end to it has already reached a critical point. This view is primarily that of outgoing AEC chairman John McCone, but it commands quite a bit of support within the commission.

The Joint Congressional Committee on Atomic Energy has generally leaned toward McCone's point of view. But no member of the committee has criticized the 8-week delay in the resumption of the Geneva talks, to the end of March, which Kennedy announced at his first press conference. That move apparently was cleared in advance with the committee, which accepted Kennedy's point that the Administration needed at least that much time to make up its mind about just what had to be done. There has been some indication that the Administration would have liked more time to prepare for the resumption of negotiations but that the 8 weeks was as much as it could get its more important potential critics to accept without raising an immediate fuss.

Nevertheless, signs of restiveness have begun to appear, and the Administration clearly is in for a hard time on this issue no matter what it decides to do. It is just not possible for a layman to reach really sound conclusions on what should be done because the information on which a decision must be based is not available to the public, and some of it, such as the effectiveness or lack of effectivness of the Central Intelligence Agency in getting wind of what is going on inside Russia, simply cannot be made available.

The difficulty of even the President's getting together enough information to provide a satisfactory basis for policy making was illustrated in the necessity at this late date of appointing a committee of scientists who have been working on the problem to provide him with what is hoped to be a definitive appraisal of the technical side of the question.

The committee included Hans Bethe, the most articulate advocate of the ban within the scientific community, but not Edward Teller, the leading opponent. This by no means implies that the report is predestined to be optimistic in tone: at the Joint Committee's test ban hearings last summer there was not much difference between Bethe's and Teller's interpretation of the technical problems of detecting clandestine tests. Both agreed that the problems were enormous.

The principal disagreement was on the amount of danger to this country's security that would be involved in risking the Russians' continued testing while we obeyed the ban. But neither man appeared to have anything like the solid factual basis for his opinions on this point that was available to lead both to agree that under any inspection system that would conceivably be accepted by the Russians it would not be easy to detect and prove a violation.

The Rules Committee

Kennedy's State of the Union message in general was completely in tone with his campaign addresses: one blunt statement after another of things that were unsatisfactory in his view, interspersed with frequent calls for action to do something about them. Here is a paragraph devoted to science and education:

"Our classrooms contain 2 million more children than they properly have room for," Kennedy said, "taught by 90,000 teachers not properly qualified to teach. One-third of our most promising high school graduates are financially unable to continue the development of their talents. The war babies of the 1940's, who overcrowded our schools in the 1950's, are now descending in the 1960's upon our colleges—and our colleges are ill prepared. We lack the scientists, the engineers, and the teachers our world obligations require. We have neglected oceanography, saline water conversion, and the basic research that lies at the root of all technological progress. Federal grants for both higher and public school education can no longer be delayed."

How much legislation to deal with these problems will actually go through Congress in this session was thrown in doubt when it became clear last week that the optimistic outlook for a reform of the Rules Committee that was reported in this space was drastically incorrect.

Speaker Rayburn was forced to postpone the showdown from Thursday of last week to Tuesday of this week in an effort to solidify support, and Kennedy, who until last week had remained aloof from the fight on the sound principle that the President should not use his personal prestige when lesser measures will do the job, gradually became more and more publicly committed on the measure, finally authorizing a spokesman to tell the press that a defeat for Rayburn on the rules change amounted to a repudiation of the President within his first two weeks in office by a Congress dominated by his own party, and that such a blow would have most unfortunate repercussions at home and abroad.

The galleries were packed when the House met for the showdown on Tuesday. Midway through the roll call the Kennedy forces trailed by a dozen votes, but at the end the rules change carried by 5 votes out of a total of 429. There was no question that the power of the Presidency had provided the narrow margin of victory. The stage was thus cleared for a burst of legislative proposals from Kennedy, but the narrowness of the margin despite the extraordinary pressures applied by Rayburn and the White House showed that the House as a whole was far from eager to begin the march into the New Frontier.

Indeed Kennedy's tactics in winning the Rules fight, together with his blunt State of the Union message, served to solidify his opposition, for there was no longer much basis for the hope that his campaign talks were just campaign talk.

But the conservative opposition was immensely weakened by the change in the Rules Committee. As the leaders on both sides clearly recognized, the issue was not entirely or even mostly the power of the committee to kill the President's program, for there are ways, albeit cumbersome ones, for a determined majority to bring bills before the House despite the opposition of the Rules Committee.

What the conservative coalition has lost that is more important is its power to keep a good part of the Kennedy program from reaching the House floor where the unique power of a President to influence public opinion through such a device as the televised press conferences could put heavy pressure on members to vote for bills they would have been quite willing to see buried in the Rules Committee.

The conservatives had much the worst of the argument on the issue, for it is hard to answer Kennedy's argument that the whole House, not six men on the Rules Committee, should have the power to vote his program up or down. But although the conservatives

were cast in the role of the "bad guys" on this issue, they did no more than what the liberals would have done if the positions had been reversed. They fought hard to avoid a disadvantageous shift in the balance of political power, and their only regret, quite properly, is that they lost.—H.M.

News Notes

U. N. Conference on Energy Sources To Meet in Rome

The United Nations Conference on New Sources of Energy, which will examine practical problems and experience in the utilization of solar energy, wind power, and geothermal energy—with especial reference to the problems of the less developed countries—will be held at the invitation of the Italian Government in Rome from 21 to 31 August 1961.

Prospects for the practical utilization of new sources of energy other than the atom were reviewed initially in a report prepared in 1957 for the United Nations Council by Secretary-General Dag Hammarskjold. In April 1959 the council decided that an international conference could yield especially interesting results for areas which have a shortage of conventional energy resources. At three preliminary meetings of experts, in Madrid, Grenoble, and Rome in May, June, and July of 1960, the program agenda and substantive guidelines for potential contributors of papers to the conference were drawn up.

Conference Agenda

The conference objective is to bring together experts in the fields of solar energy, wind power, and geothermal energy, as well as people interested in energy development in general, to provide participants with up-to-date information on progress, problems, potentialities, and limitations in utilizing these three sources of energy, especially in areas lacking conventional energy sources or facing high energy costs. Participants in the conference, who will attend as individuals and not as representatives of governments, organizations, or societies, will emphasize applications of these forms of energy rather than scientific principles or basic research.

The agenda provide for two parallel series of technical discussions, one devoted basically to the utilization of geothermal energy, wind power, and solar energy for power purposes, the other to solar energy for purposes other than power.

Participation will be by invitation of the U.N. Secretary-General. Participants will be selected from among duly qualified persons who have been nominated to attend. Nominations will be made by governments of member states or their governmental services, by the United Nations and its specialized agencies, and by interested nongovernmental organizations or societies. It is expected that qualified individuals will also apply for invitations, and their requests will receive particular attention.

As a result of the preliminary meetings in 1960, some specialists have already been asked to submit papers. In addition, the Secretary-General is inviting 16 outstanding specialists to serve as rapporteurs on agenda items. A rapporteur will introduce the subject for which he is responsible, having first reviewed the papers contributed in that area and prepared a general report suggesting the main lines for discussion. In addition, the rapporteurs will summarize problems and findings in the plenary meetings. Before the meeting, they will also screen papers and advise the secretariat in preparatory work.

The United Nations has issued an information bulletin covering organizational arrangements for the conference and including application forms for participation. The Secretary-General has appointed Alfred G. Katzin of his office to be executive secretary of the conference.

Harvard Sponsoring Program on Science and Public Policy

The Graduate School of Public Administration of Harvard University, with the aid of a grant from the Rockefeller Foundation, has undertaken a research and training program on science and public policy, including an unusual seminar for advanced students that is in its first year of operation. The level of the seminar is apparent from a list of some of the 1960–61 guest speakers: former presidential science adviser George B. Kistiakowsky; Admiral Rawson Bennett, the retiring head of the Office of Naval Research; Elting E. Morison of Massachusetts Institute of Technology; Caryl P. Haskins of the Carnegie Institution of Washington; Major General James McCormack, USAF (retired), vice-president of M.I.T.; and Sir Charles P. Snow, physicist and author and former United Kingdom Civil Service commissioner.

Admission to the Seminar

About 15 students are admitted to the seminar each year. As in other research seminars of the school, students are selected primarily from among candidates who have had a number of years of experience in government or in comparable research or administrative positions and who seek to prepare themselves to deal with public policy issues at a higher level of responsibility.

Seminar participants are expected to make a contribution to the study of some aspect of the broad range of problems involved in the application of science to the formulation and determination of public policy, and in the financing and administration of scientific research. Admission is based on a man's academic record, including graduate work, if any; on public service experience; and on recommendations, especially from his government agency if he has been selected by it for training.

The breadth and flexibility of the school's programs make them especially appropriate for men in those government agencies which, because many of their leaders in administration and policy are drawn from technical or professional fields, seek to combine technical training and scientific research with executive development. A student who wishes to participate in the research seminar in science and public policy will be considered for admission regardless of his intention to qualify for a degree.

Fellowships

All federal and certain other public agencies have authority to pay expenses for advanced training at nongovernment institutions, where this is part of the agency's approved training program. Employees of such agencies are encouraged to investigate their eligibility for such training before applying for admission.

Several fellowships are available for candidates who are not eligible for training at government expense. Fellowship stipends will be sufficient to cover tuition and, on the basis of need, most of a student's living expenses.

Application blanks, catalogs, and

other information may be obtained by writing to the Registrar, 123 Littauer Center, Harvard University, Cambridge 38, Mass. Applications for admission for the academic year 1961–62 are *due on 15 March*, but late submission can be arranged, especially if advance notice is given informally by candidates selected by government agencies for advanced training. The academic year 1961–62 will begin 5 September and end 5 June.

Member of Scott's Last Expedition Returns to Antarctic after 47 Years

Sir Charles S. Wright, a member of the ill-fated 1911–1913 expedition of Robert Falcon Scott, has returned to Antarctica as a scientist with the U.S. Antarctic Research Program. A Canadian member of Scott's expedition, Sir Charles was one of the party that on 12 November 1912 discovered the bodies of Scott and three companions, who had perished on the return trek from the South Pole when beset by blizzards and the approaching winter.

Sir Charles, a physicist with the Pacific Naval Laboratories, Canadian Defense Research Board, is on loan to Stanford University to participate in a joint Stanford-PNR study of very low frequency radio waves. His return to the Antarctic was arranged by the National Science Foundation, which manages the U.S. scientific program there. His transport was provided by the U.S. Navy, responsible for logistic support of the science program.

The Stanford-PNR study involves work at Byrd Station, Antarctica, by Sir Charles and Donald J. Evans, and at Great Whale River, Canada—Byrd's conjugate point—by Stanford personnel. Stanford has received an NSF grant of $59,740 in support of the work.

NASA Setting up Institute for Space Studies

The National Aeronautics and Space Administration is establishing a theoretical research group in New York City. Designated the Goddard Institute for Space Studies, the group will serve as an arm of the Theoretical Division of the Goddard Space Flight Center, located at Greenbelt, Md. Robert Jastrow will serve as director of the institute and will also remain in his present position as chief of the Theoretical Division at Goddard.

The institute will begin formal operations in May 1961. Its staff of approximately 50 will work in close association with universities and research institutions in the New York area. An office site has not yet been selected.

The regular staff will be supplemented by scientists from nearby universities, who will be appointed on a part-time consulting basis to participate in the research program. Such appointments for part-time research have been accepted by Maurice Ewing of Columbia University and Bëngt Strömgren of the Institute for Advanced Study at Princeton.

The program of the institute will include basic theoretical research in fields having a bearing on the NASA space science program. Major areas of activity in the program will be the structure of the earth, the moon, and other planetary bodies in the solar system; the atmospheres of the earth and other planets; the origin and evolution of the solar system; the properties of the interplanetary plasma; sun-earth relationships; celestial mechanics; and the structure and evolution of the stars.

Heart Association Reports More Research Support Needed

The American Heart Association has contradicted published statements that the availability of funds for medical research has outstripped the availability of qualified investigators to use them properly. In its 1960 annual report, issued on 26 January, the association declares that "double the sums now available could be used effectively to speed conquest of heart disease."

Quoting its national research committee, the association urges that every aspect of research support be expanded and essential new programs be added. At the same time, the report emphasizes that the largest share of the association's expenditure in fiscal year 1959–60—$9,053,592 out of a total of $24,377,435—was assigned to support of scientific research.

The report notes further that despite this record-breaking research allotment, funds were lacking to support all grants approved as scientifically worth while by the research committee. Forty-two applications had to be denied outright, sums requested for grants-in-aid were cut by one-third, and the number of new "career investigator" appointments had to be limited to two—"although many excellent candidates are considered deserving in this most important area." The career investigatorship provides lifetime research support for outstanding scientists working in the broad field of heart and blood-vessel diseases.

Sir Charles Wright visits the darkroom of Scott's hut at Cape Evans, Antarctica. This darkroom was used by the famous Antarctic photographer Herbert Ponting during the Scott 1911–1913 expedition, of which Sir Charles was a member.

In an introduction to the report, Oglesby Paul of Chicago, association president, emphasized the need for major expansion in all aspects of the program to combat cardiovascular disease.

News Briefs

Business aids education. Twenty-one Cleveland business firms will give a minimum of 1 percent of their income (before taxes) to help higher education during the next 3 years. In "A Proposal to Those Who Believe in American Leadership," the company leaders called on business and industry to follow their example. The aid planned may take the form of grants for capital construction, unrestricted operating grants, endowed chairs, or funds to match alumni contributions by employees.

According to recent estimates, corporation aid to higher education amounts to $150 million, representing one-third of 1 percent of earnings before taxes. The Council for Financial Aid to Education, whose studies have indicated the need for increased business support for higher education, cooperated in working out the new program.

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Meteorite collection. Arizona State University recently purchased the Nininger Meteorite Collection with the financial assistance of a private donor, the National Science Foundation, and the Arizona State University Foundation. The collection contains 1220 catalogued specimens, plus several thousand small particles, from 684 of the 1600 known meteorite falls. The material will be available to scientists but not to the lay public. Carleton Moore of Wesleyan University has accepted the directorship of the Nininger Meteorite Laboratory and will join the Arizona faculty in June.

In connection with the collection, a symposium on meteorites will be held on 10 March as part of the inauguration ceremony for G. Homer Durham, the university's new president. Papers for the symposium should be sent to Dr. Carleton Moore, Wesleyan University, Middletown, Conn. He will edit the symposium volume, with the assistance of an advisory board.

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Industrial science award. During the recent AAAS meetings the association's Industrial Science Section presented its annual Industrial Science Achievement Award to the Bell Telephone Laboratories for its work in the field of universal communication during the year 1960. Among the advances cited were the successful experiments in long-distance communication through reflection of radio signals from the satellite Echo I (conducted in cooperation with NASA); the development of a new switching system that more than doubles the message-carrying capacity of existing submarine cable facilities; and development of the first electronic telephone switching system, which was placed in full-time experimental service at Morris, Ill., in November 1960.

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NASA life sciences laboratory. A Life Sciences Research Laboratory was opened at the National Aeronautics and Space Administration's Ames Research Center, Moffett Field, Calif., on 1 February. Clark T. Randt, director of the NASA Office of Life Sciences Programs, says the installation at Ames will eventually have a staff of 60 scientists and some 140 supporting technicians.

The new facility was opened with the assignment of Richard S. Young as chief of the Environmental Biology Branch. The laboratory will be headed by a director who will serve as assistant director to Smith J. DeFrance, now in charge of the Ames Research Center. Under the laboratory director there will be three divisions—flight medicine and biology, space medical and behavioral sciences, and space biology.

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History of science. At a recent meeting of the George Sarton Memorial Foundation it was announced that funds are being sought to obtain a distinguished historian of science from abroad to be a featured speaker at the 10th International Congress for the History of Science, to be held at Cornell University and in Philadelphia in 1962. The foundation also announced its intention to maintain funds for a featured speaker on the history and philosophy of science at the AAAS annual meetings. Retiring AAAS president Chauncey D. Leake, of Ohio State University, is the foundation's new president.

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Japanese satellite. Japan has announced that it will inaugurate a space program this year and plans to launch an earth satellite by 1963. This would be sent into orbit with American rockets from a site in the United States.

Grants, Fellowships and Awards

Allergy. The Scientific and Educational Council of the Allergy Foundation of America has announced the availability of a limited number of quarterly or summer scholarships at $600 each in approved medical schools in the United States and Canada. The awards, for students who have completed their second or third year in medical school, are to support a minimum of 8 weeks of training in both clinical and research aspects of allergy.

Each medical school is invited to submit the name of one applicant through the dean's office, accompanied by a supporting letter from the dean. Applications should be sent *by 1 March* to Dr. William B. Sherman, Chairman, Scientific & Educational Council, Allergy Foundation of America, 801 2nd Ave., New York 17, N.Y.

Hydromechanics. The Navy's David Taylor Model Basin has announced that proposals for the Bureau of Ships Fundamental Hydromechanics Research Program for the next fiscal year should be received *by 15 March.* Areas of interest are resistance, propulsion, stability, control, sea-keeping characteristics, radiation of underwater sound, and other hydromechanics problems which may be applicable to all types of Navy craft. Information concerning the program may be obtained by writing to the Commanding Officer and Director, David Taylor Model Basin, attention Contract Research Administrator (Code 513), Washington 7, D.C.

Laboratory development. The National Science Foundation has announced that *1 March* is the next closing date for receipt of proposals in the Graduate Laboratory Development Program. This program requires at least 50-percent participation by the institution with funds derived from nonfederal sources.

The purpose of the grants is to aid institutions of higher education in modernizing, renovating, or expanding graduate-level basic research laboratories used by staff members and graduate students. Only those departments having an on-going graduate training program leading to the doctoral degree in science at the time the proposal is submitted are eligible at present. Proposals, as well as requests for additional information, should be addressed to: Office of Institutional Programs, NSF, Washington 25, D.C.

Scientists in the News

Louis P. Hammett, physical chemist of Columbia University, has won the 1961 Willard Gibbs Medal of the American Chemical Society's Chicago Section. The award is made annually to a scientist "who, because of his eminent work in, and original contributions to, pure and applied chemistry, is deemed worthy of special recognition."

Hammett will receive the medal on 19 May at a dinner celebrating the 50th presentation. He is being honored for having laid the foundations of modern physical organic chemistry and for his outstanding record as a teacher, administrator, and research worker. Hammett, who also won the ACS Priestly Medal for 1961, is the newly elected chairman of the society's board of directors.

Frank T. McClure, chairman of the Research Center at the Johns Hopkins University Applied Physics Laboratory, Silver Spring, Md., recently received a $3000 award from the National Aeronautics and Space Administration for his invention of a satellite Doppler navigation system. The award was the first made under the invention award authority of the 1958 Space Act. McClure's invention was basic to the Navy Department's navigational satellite program, Project Transit.

Curt Stern of the University of California, Berkeley, is the new president-elect of the American Society of Zoologists. He replaces **C. Ladd Prosser**, who has become president.

Ray D. Owen, geneticist and immunologist, has been appointed acting chairman of the Biology Division of the California Institute of Technology. He succeeds Nobel laureate **George W. Beadle**, who is leaving to become chancellor of the University of Chicago.

Milton J. Schiffrin has been appointed director of clinical research, Medical Research Department, Hoffman-La Roche, Inc., Nutley, N.J. He has been at the firm's Chicago regional office for the past 15 years. In his new post he will supervise the activities of the company's regional medical offices in Houston, Tex., San Francisco, Calif., and Chicago, Ill.

Garrison Cattell and **Dorothy Hancock** succeed the late Jaques Cattell as editors of *American Men of Science*.

Elmer McCollum, emeritus professor of biochemistry at Johns Hopkins University, received the New York Academy of Medicine Medal on 5 January "in recognition of his basic research which ushered in the era of the newer knowledge of nutrition; of his fruitful efforts which contributed to the eradication of deficiency diseases; of his demonstration of the tremendous significance of nutrition . . . for the promotion of health and prolongation of life; and of his influence upon the dietary habits of man throughout the world, through his research, writing and teaching." This was the 15th presentation of the medal in 32 years.

The 1960 Franz Alexander Prize of the Chicago Institute for Psychoanalysis was awarded on 25 January to **W. Donald Ross** and **Frederic T. Kapp**, associate professors of psychiatry at the Univerity of Cincinnati, for their paper, "A technique for self-analysis of countertransference."

Marcus Singer, professor of zoology and of child development and family relationships at Cornell University, has been named Henry Willson Payne professor of anatomy and director of the department in the School of Medicine at Western Reserve University. Also at Western Reserve, **Howard A. Schneiderman**, now associate professor of biology at Cornell, has been appointed professor of biology. Both appointments will become effective on 1 July.

A. B. Cambel, chairman of the mechanical engineering department at Northwestern University, will tour as a national lecturer of the Society of Sigma Xi during the 1961–62 academic year. He will speak on magneto-gas dynamics.

The American Meteorological Society has announced the election of a new president and vice president—respectively, **Thomas F. Malone**, director of research for the Travelers Insurance Company, Hartford, Conn., and **Patrick D. McTaggart-Cowan**, director of the Canadian Meteorological Service, Toronto, Ontario.

The China Medical Board of New York, Inc., has announced that **Kenneth L. Duke**, associate professor of anatomy at Duke University School of Medicine, has been selected as the recipient of the 1961 Alan Gregg Travel Fellowship in Medical Education. Duke plans to make a comparative histological study of the ovaries of mammals in Southeast Asia. He will spend approximately 6 months in that area, mostly at the University of Malaya.

Hugh Bradner, of the Lawrence Radiation Laboratory at the University of California, received an honorary degree from Miami University on 29 January, when he was the speaker at ceremonies of mid-year graduation and dedication of a new science building.

Ralph C. Graber has been named assistant chief of the U.S. Public Health Service's newly formed Division of Air Pollution. Formerly he was chief of the Air Pollution Engineering Services, an agency no longer in existence.

Abraham Hyatt has been named director of the National Aeronautics and Space Administration's Office of Program Planning and Evaluation. He succeeds **Homer J. Stewart**, who has returned to his professorship at the California Institute of Technology, Pasadena. Previously Hyatt was deputy director of NASA's Launch Vehicle Programs.

Recent Deaths

Ralph L. Belknap, Ann Arbor, Mich.; 62; associate professor of geology at the University of Michigan; 17 Dec.

Francesco Giordani, Naples, Italy; 64; professor of general and inorganic chemistry at the University of Naples and former president of the Italian National Committee for Nuclear Research; in 1956–57, helped lay the groundwork for Euratom, the six-nation European nuclear energy community; 24 Jan.

Irving Lorge, New York, N.Y.; 55; professor of education and executive officer of the Institute of Psychological Research at Teachers College, Columbia University; leader in psychological testing who, in collaboration with the late E. L. Thorndike, developed the Lorge-Thorndike Intelligence Test; 23 Jan.

Abraham I. Rubenstone, Philadelphia, Pa.; 71; professor emeritus of clinical medicine at Hahnemann Medical College and former chief of medical service at Einstein Center, Southern Division; 22 Jan.

Wayland F. Vaughan, Needham, Mass.; 59; professor of psychology at Boston University and head of the department from 1934 to 1946; 21 Jan.

Book Reviews

The Ethical Animal. C. H. Waddington. Allen and Unwin, London, 1960. 230 pp. 25s.

This is a notable book on an important subject, written by an outstanding scientist and thinker. What it is about is concisely stated on page 23: "It is the thesis of this book that the framework within which one can carry on a rational discussion of different systems of ethics, and make comparisons of their various merits and demerits, is to be found in a consideration of animal and human evolution." This idea is not quite new; it was stated previously in Waddington's well-known *Science and Ethics* (1942). Rather closely related but not identical ideas were advanced by Chauncey Leake; they have been made popular in numerous writings by Julian Huxley. The book under review is, nevertheless, the first in which the argument is developed fully, explicitly, and with admirable clarity, so that its strong and weak points can be clearly identified and subjected to analysis and criticism.

Of the 16 chapters into which the book is divided, four are the crucial ones (chapters 2, 12, 13, and 14). Waddington takes as his point of departure this fact: "For every human being there are some propositions which he considers to be ethical, that is to say, to relate to goodness and badness or duty and obligation." Waddington does not attempt to define goodness in terms of other concepts, such as pleasurableness, desirability, and so forth. He considers, instead, the ontogeny of the concept of the good, that is, the developmental processes which lead to its formation in a human individual. He suggests that there is an early developmental stage at which an infant becomes an "authority-acceptor" and an "ethicizing being," and he supports this suggestion by referring to the work of psychologists and psychoanalysts who have studied the development of the human personality. Waddington then argues very cogently that the capacity to accept authority and to acquire ethical beliefs is established in human biological evolution as an essential adaptation for transmitting from one generation to another the store of information which constitutes human culture. But as so often happens in evolution, a highly adaptive functional system has some features which by themselves are unadaptive: "Some development of 'authority-bearing systems' is, as we have said, necessary to mold the baby into an information-acceptor," and yet "the processes which the human species has evolved for bringing about this result are of a kind which will almost inevitably lead to an over-development of authority." As a consequence, "we tend to demand of our ethical beliefs a degree of certainty which we would never look for in any other doctrines. They should, we feel, be universal in scope, absolute in character and unassailable in validity." To me, an essential, and an attractive, feature of Waddington's theory is the emphasis he places on the fact that it is the ability to "ethicize," and not the contents of the ethical beliefs, that is a product of adaptation in the process of biological evolution. The theory thus avoids the pitfall of supposing that there exist genes for transmitting this or that ethical tendency or belief, a supposition at variance with our present ideas about the role of genes in development and in evolution.

Criterion of Biological Wisdom

Waddington's attempt to find an evolutionary criterion for evaluating ethical beliefs is very ingenious. The basic argument here is that the biological "function of ethicizing is to make possible human evolution in the sociogenetic mode." However, "To say that something has a function is not merely to assign causal efficacy to it, but implies further that the causal network of which it is a part has as a whole some general character. A particular example of the activity can then be judged by how well it brings about the realization of that character." Here, then, Waddington sees a criterion for criticizing the validity of ethical systems. Provided that we discover the general character of human evolution and, indeed, of the evolution of life as a whole, "We have then to inquire, of any particular ethical belief which comes to our attention, how effective it is in mediating this empirically ascertained course of evolutionary change." This is what the author calls the criterion of biological wisdom. *Wisdom* used in this metaphorical sense (parallel to Cannon's "wisdom of the body" or "homeostasis") is not necessarily the same as *wisdom* in philosophical discourse or in everyday life. This is probably the Achilles' heel of the theory; I find myself unable to accept the conclusion drawn by Waddington: "One could, therefore, not question the wisdom of evolutionary advance since this is a matter of definition." Nor is the problem of the general direction of biological and of human evolution an easy one. Waddington argues: "Biological wisdom consists in the encouragement of the forward progress (anagenesis) both of the mechanism of the socio-genetic evolutionary system, and of the changes in the grade of human organization which that system brings about. . . . The general anagenesis of evolution is towards what may crudely be called richness of experience." He wisely refrains from an "attempt to work out, even in broad outline, the nature of the conclusions to which the application of the evolutionary criteria would lead."

Waddington is well aware that a biologist writing about ethics is likely to find himself in a position "like a baby sitting in the bath water, called upon to parry the attacks of well-meaning philosophers anxious to resolve semantic puzzles by emptying me, along with a lot of other alleged rubbish, down the sink." He defies these well-meaning efforts and shows that he is at least aware of the objections raised against "scientific" ethics by philosophers from Hume (who pointed out that one cannot logically pass from "is" to "ought") to the modern logical positivists (dealt with in a chapter entitled "Squaring the Vienna circle"). In another chapter, "Understanding and believing," Waddington takes up matters of *wisdom* in its more usual sense and concludes: "The authority of science gives its sanction to one of the greatest creations of the human mind—the attitude of logical thought continually checked by the empirical appeal to experiment—but it needs, in my view, to be supplemented

by the ideal of the creative artist—an ideal which expresses itself in thought precesses which move in a different dimension to those of logic and experiment." One can only hope that this wisdom can be squared with the *wisdom* of the evolutionary process.

The theory presented in *The Ethical Animal* will not, as Waddington is well aware, be accepted unanimously by everybody, or even by all biologists. It is nevertheless a significant contribution to the discussion of a momentous issue. By changing what he knows about the world, man changes the world he knows; by changing the world, he changes himself. Are these changes in accord with biological and other wisdom?

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Geological Survey Research 1960. Professional Paper No. 400, part A and part B. U.S. Geological Survey, Washington, D.C., 1960 (order from Supt. of Documents, GPO, Washington 25). Part A, 142 pp., illus., $1; part B, 523 pp., illus., $4.25.

The United States Geological Survey is currently engaged in so many activities and projects, spanning the full range of the geological sciences, that publication of results has tended to lag behind the completion of many investigations. This book has been prepared to make available a digest of important new ideas and new discoveries, both published and unpublished, made by survey personnel during the 12 months that ended 30 June 1960. This presentation is an experimental one, and only the work of the Geological Division is included.

The arrangement of material is dictated by what the Geological Division considers to be its major objectives: increasing our knowledge in economic geology, regional geology, and geologic principles and processes. Pages A1–A26 are devoted to economic problems, by district and region, together with commodity and topical studies. Many persons outside geology will consider this to be the most important phase of the survey's work, because the economic studies help in solving problems connected with the construction of highways and dams and, while developing information in the search for new deposits of minerals and fuels, provide the nation with a continuing appraisal of its known and potential mineral and fuel resources. It should be noted, however, that without the supporting regional studies (pages A26–A54) and those that deal mainly with principles and processes (pages A54–A73), the specific economic studies would soon become sterile.

All reports and articles by survey personnel, actually published or otherwise released to the public during fiscal 1960, are listed alphabetically by author in the bibliography (pages A107–A127). Not every title that will eventually bear dates between July 1959 and June 1960 could be included, since publication in periodicals is commonly delayed several months. The inclusion of journal articles and survey open-file reports with standard survey publications will greatly aid geologists and others searching the recent literature. The "Subject classification of publications" (pages A127–A136), together with the very detailed table of contents, makes the lack of a general index less inconvenient.

The list of investigations now in progress, which gives the name and headquarters of those in charge of each investigation (pages A77–A105), alone makes the publication worth the price. Too often in the past, even after extensive inquiry, have workers outside the survey started a research project only to find that it duplicated a survey project which was well under way. The only illustrations in part A are four index maps.

The second part of this professional paper is bound separately and consists of 232 papers, generally of less than 1000 words each. Some of the papers are primarily announcements of new discoveries or observations on problems of limited scope, and for many, this will probably be the final report. Others are progress reports on more extensive investigations which have been under way for some time. It is expected that these conclusions will, in large part, be included in much longer reports to be published when the projects are complete.

Most authors are represented by one paper, but some have as many as seven. The papers, well-illustrated by line drawings and a few photographs, are arranged, as to subject matter, in the same order as those in part A. The volume has a comprehensive index, by subject and author, referring to article number rather than to page.

I hope that the publication will be continued and that it will be expanded to include the work of other survey divisions.

Obviously few, if any, will read the entire book but almost every geologist will enjoy and benefit by browsing, not only in his own field of interest but also in the many others presented. There is a wealth of material for the teacher and the research geologist, as well as for those more concerned with practical application of the science.

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Analysis and Design of Feedback Control Systems (formerly *Servomechanism Analysis*). George J. Thaler and Robert G. Brown. McGraw-Hill, New York, ed. 2, 1960. xiii + 648 pp. Illus. $14.50.

The first industrial revolution provided abundant power for operating machinery, but this power had to be controlled by human beings. In the present industrial revolution, more and more of the control functions are being taken over by the machines themselves. This is done by using the principle of feedback. A standard is set up for the variable to be controlled in an industrial process. This standard is continuously compared with the actual value of the variable, and an error signal is obtained, which is then used to actuate machinery in such a way that the error is reduced.

The present volume is intended for use by electrical engineering students who are taking the analysis and design of such apparatus at the senior or graduate level. The authors first provide an introduction to the subject and some of the basic working tools. They then deal with the analysis of linear control systems: how to evaluate their performance—the speed of response, stability, overshoot, steady-state error, and so forth. They continue with the design and construction of control systems for given specifications. Finally they go on to more advanced aspects of the subject and discuss Mitrovic's method, sampled data control systems, and the analysis and design of nonlinear control systems, including relay servomechanisms. There are five appendixes, giving, in addition to some useful tables, descriptions of physical components

such as error detectors, motors, and hydraulic and pneumatic devices.

I especially enjoyed the two chapters on the design of linear systems. Here the authors include down-to-earth advice: "Once a design has been made acceptable by changes which satisfy test conditions, further changes should be avoided. It often happens that additional changes are requested in order to further improve performance, lower cost, etc. Such changes seem insignificant and unrelated to sources of trouble, but often prove very unwise." They also provide a step-by-step discussion of the design of several control systems which were actually built. The volume contains a large number of exercises for the students, and reflects throughout the authors' experience, both in the classroom and on the workbench. It should serve its intended purpose admirably.

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Cultivated Palms. Special issue of *The American Horticultural Magazine*. R. Bruce Ledin, Guest Ed. American Horticultural Society, Washington 2, D.C., 1961. 189 pp. Illus. Paper, $3.

The general thesis of this handbook on the palms is "what the plants look like taxonomically and horticulturally . . . how to grow the plants. . . . [and] the difficulties that may arise" in cultivation. The idea of preparing such a volume was presented by W. H. Hodge to the executive committee of the Palm Society when he was president of the society.

The material is divided into three sections: "An introduction to the palms," "Culture of palms," and "Uses of palms." The first section includes a paper by Hodge, entitled "The world of palms," eight pages (containing 32 illustrations) showing palm characteristics (fruit clusters; palm flowers, leaves, and stems; and others), a series of 80 full-page illustrations, arranged alphabetically by botanical name, called "Palm portraits," as well as other illustrations and papers.

The second and third sections contain 16 contributed papers, a check list of palms known to be growing in Hawaii (by L. W. Bryan), a list (one page) of living palm collections, and an index of palm names.

The Bradley Volume. A special volume of the *American Journal of Science* in appreciation of Wilmot Hyde Bradley on his sixty-first birthday. American Journal of Science, Sterling Tower, New Haven, Conn., 1960. 433 pp. Illus. $4.75.

The Bradley Volume comprises 38 papers dealing with modern geologic science, written by 48 authors who hail from a dozen or so different institutions. This fine collection honors Wilmot Hyde Bradley who, as chief geologist of the U.S. Geological Survey from 1944 to 1959, directed an inspired program by the Geologic Division, a program that constantly sought and explored new vistas in geologic research. Traditionally the survey's forte has been the investigation of geologic problems by means of surface and subsurface detailed mapping and attendant topical studies. Bradley, dedicated to the growing importance of the interdisciplinary connections of geology with chemistry, physics, biology, and engineering, created within the survey another forte that is currently being maintained by a staff of vigorous young scientists who are setting the stage for future break-throughs in the understanding of geologic processes. It is this contribution to the development of the science and of the survey's research program that is the true focus of *The Bradley Volume*; accordingly, the assembled papers represent a spectrum of inquiry which recreates the image of this enlightened leader.

To list the papers by title or to comment on their excellence would be tedious. The book has no central theme other than the breadth of geology itself, as expressed in these short papers. Strong emphasis emerges on the experimental, theoretical, and philosophical aspects of the subject matter. In the papers dealing with geochemistry and geophysics, for example, measurements per se are stepping stones en route to the formulation of conclusions in crystal chemistry, mineral genesis, solution chemistry, and mineral stability in natural environments. Field observations and compilations, set forth in detail or graphically summarized, lead to the philosophical treatment of crustal formation, rock alteration, distribution of elements, and the petrologic history of igneous, metamorphic, and sedimentary rocks. Biological inquiry is used to develop perspective on organic resemblance and evolution, stratigraphic and zoogeographic distribution, and paleoecology and sedimentary basins.

Although the individual specialist may find only a few papers in his field within this volume, the whole is much more than the sum of its parts; the assemblage represents a formidable sampling of modern geology, which brings credit to the *American Journal of Science* for its role in sponsoring *The Bradley Volume*. Certainly the volume brings great pride and pleasure to those of us who find that it is also a fitting tribute to Bill Bradley's keen sense of human values which underscores his concept of a creative research community. If you are interested in what modern geologists are thinking and writing about, you will want your own copy.

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The Rich and the Poor. A study of the economics of rising expectations. Robert Theobald. Potter, New York, 1960. 196 pp. $4.50.

The title suggests that this book could have been written 100 years ago when farsighted people in industrial countries were concerned with the broad gulf between the rich and the poor and when, in several countries, conservative statesmen urged the adoption of progressive taxation and social policy measures in order to forestall a revolt of the poor. They did it because of humanitarian motives and enlightened self-interest. They knew that a small group of rich people could not survive surrounded by hopeless poverty.

A very similar appeal, to both humanitarian motives and enlightened self-interest, is now addressed to the rich countries urging them to pursue a more vigorous policy in support of economic development in the poor countries. In this respect Theobald adds his voice to many others who have felt the same sense of urgency.

Most interesting is his elaboration of the thesis that different economic reasoning should apply to the industrially advanced and the underdeveloped countries. He points out, for instance, that even relatively stiff progressive income taxes do not seriously interfere with incentives to great effort or with the necessary capital formation in the industrial countries. If poor countries

in early stages of development follow the advice, frequently given to them, that they too should adopt a progressive tax system, they may seriously interfere with their economic development. The author warns against applying policies which may be suitable for one group of countries to the other group without full consideration of the differences in motivation, value systems, and institutions. His pet peeve is the neoclassical approach to economics, which believes that there is a truth in economics applicable to all countries and conditions.

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Die Entdeckung neuer Organisationstypen im Tierreich. *Die Neue Brehm-Bücherei,* No. 258. Peter Ax. Ziemsen, Wittenberg, East Germany. 1960. 116 pp. Illus. DM. 6.50 (approximately $1.60).

This small paperback in the "Neue Brehm-Bücherei" series is packed with information on a wide variety of recently discovered and unusual animal types, including *Neopilina,* Pogonophora, *Halammohydra, Monobryozoon,* Mystacocarida, Cephalocarida, Xenoturbellida, Gnathostomulida, Monotoplanidae, Polystyliphoridae, and *Latimeria.* The text is richly illustrated, well written, concise, and scholarly; where appropriate, emphasis is placed on morphology, physiology, ecology, or phylogeny. There are 104 references to a greatly scattered literature. Every serious Ph.D. candidate in invertebrate zoology should have this excellent little book.

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New Books

Mathematics, Physical Sciences, and Engineering

Aerodynamic Capture of Particles. E. G. Richardson, Ed. Pergamon, New York, 1960. 208 pp. Illus. $8. Proceedings of a conference held by the British Coal Utilization Research Association at Leatherhead in 1960; the discussion covers theoretical and fundamental aspects, experimental application of capture techniques, and capture of particles by raindrops.

Block and Graft Polymers. William J. Burlant and Allan S. Hoffman. Reinhold, New York; Chapman and Hall, London, 1960. 172 pp. Illus. $7.95.

Cobalt. Its chemistry, metallurgy, and uses. Roland S. Young, Ed. Reinhold, New York; Chapman and Hall, London, 1960. 431 pp. Illus. $15. "This new book replaces . . . monograph No. 108 *Cobalt,* written by the present Editor."

Extractive and Physical Metallurgy of Plutonium and Its Alloys. Including a special introduction and annotated bibliography. W. D. Wilkinson, Ed. Interscience, New York, 1960. 324 pp. Illus. $10.50. Based on a symposium (16–17 February 1959) sponsored by the Metallurgical Society and the American Institute of Mining, Metallurgical, and Petroleum Engineers.

Field Theory of Guided Waves. Robert E. Collin. McGraw-Hill, New York, 1960. 619 pp. Illus. $16.50.

The Mysterious Earth. Lester Del Rey. Chilton, Philadelphia, Pa., 1960. 226 pp. $2.95.

The New Age in Physics. Sir Harrie Massey. Harper, New York, 1960. 342 pp. Illus. + plates. $5.

Official Methods of Analysis of the Association of Official Agricultural Chemists. William Horwitz, Ed. The Association, Box 540, Benjamin Franklin Sta., Washington, D.C., ed. 9, 1960. 852 pp. Illus. $17.50.

Phosphorus Metabolism of Brain. P. J. Heald. Pergamon, New York, 1960. 202 pp. Illus. $6.50.

Physical Methods of Organic Chemistry. vol. 1, pt. 3. Arnold Weissberger, Ed. Interscience, New York, 1960. 860 pp. $24.50.

Polystyrene. William C. Teach and George Kiessling. Reinhold, New York; Chapman and Hall, London, 1960. 187 pp. $5.

Principles of Meteoritics. E. L. Krinov. Translated by Irene Vidziunas. Translation edited by Harrison Brown. Pergamon, New York, 1960. 546 pp. Illus. $12.

Pulp and Paper. Chemistry and chemical technology. vol. 3, *Papermaking.* James P. Casey. Interscience, New York, ed. 2, 1960. 337 pp. Illus. $25.

Pure Mathematics. A university and college course. vol. 1, *Calculus.* F. Gerrish. Cambridge Univ. Press, New York, 1960. 409 pp. Illus. $5.

Qualitative Theory of Differential Equations. V. V. Nemytskii and V. V. Stepanov. Princeton Univ. Press, Princeton, N.J., 1960. 531 pp. Illus. $12.50.

Radiation Chemistry of Organic Compounds. A. J. Swallow. Pergamon, New York, 1960. 389 pp. Illus. + plates. $15.

Sixth National Symposium on Vacuum Technology, Transactions, 1959. Also cumulative index of 1954–1959 symposia. C. Robert Meissner, Ed. Pergamon, New York, 1960. 335 pp. Illus. $17.50. Contents: 58 papers presented at the annual symposium; index A in which titles of papers presented at previous symposia are arranged in chronological order; index B, in which authors and coauthors are listed alphabetically.

Solid Propellant Rocket Research. Martin Summerfield, Ed. Academic Press, New York, 1960. 711 pp. Illus. $6.50.

Solution of Equations and Systems of Equations. A. M. Ostrowski. Academic Press, New York, 1960. 211 pp. Illus. $6.80.

The Solubility Product Principle. An introduction to its uses and limitations. S. Lewin. Interscience, New York, 1960. 129 pp. Illus. $3.50.

Space Trajectories. A symposium sponsored by the American Astronautical Society, the Advanced Research Projects Agency, and Radiation Incorporated. T. C. Helvey, Symposium Chairman. Academic Press, New York, 1960. 308 pp. Illus. $12.

Specification and Engineering Writer's Manual. Thomas S. Sawyer. Nelson-Hall, Chicago, Ill., 1960. 231 pp. $6.95.

Tables of Thermodynamic and Transport Properties of Air, Argon, Carbon Dioxide, Carbon Monoxide, Hydrogen, Nitrogen, Oxygen, and Steam. Joseph Hilsenrath *et al.* Pergamon, New York, 1960. 491 pp. $20. A revised collection of tables originally published by the U.S. National Bureau of Standards as *Tables of Thermal Properties of Gases* (Circular 564).

The Use of Organic Reagents in Inorganic Analysis. A. I. Busev and N. G. Polianskii. Translated from the Russian by J. T. Greaves. Pergamon, New York, 1960. 82 pp. $3.50.

Ultraviolet Guide to Minerals. A complete working manual for the use of ultraviolet light in locating and recognizing minerals. Including field identification charts. Sterling Gleason. Van Nostrand, Princeton, N.J., 1960. 256 pp. Illus. + plates. $6.95.

Waves in Layered Media. Leonid M. Brekhovskikh. Translated from the Russian by David Lieberman. Academic Press, New York, 1960. 571 pp. Illus. $16.

References and Bibliography

The International Who's Who, 1960. Europa Publications, London, ed. 24, 1960. 1053 pp. $22.

Scandinavian Research Guide. Directory of research institutions within technology and science, exclusive of life sciences. Scandinavian Council for Applied Research, Blindern, Norway, 1960. 2 volumes (approximately 800 pp.). $10. The guide, intended as a source of information on the following types of institutions—governmental, semigovernmental and cooperative institutes, and private laboratories which undertake contract work for others—covers institutions in Denmark, Sweden, Iceland, Norway, and Finland. Volume 1 (approximately 680 pages) provides a list of research institutes and laboratories arranged by subject—for example, mathematics, biosciences, and building. Information supplied about each organization includes its affiliation, the name of the head of the organization, the number and type of its staff members, and its research activities and publications. Volume 2 covers the following types of organizations: central research organizations, universities and institutes of technology, scientific societies (and their publications), central scientific and technical libraries and information services, and productivity centers. It also contains a bibliography, and three indexes—subject, institutional, and persons.

Reports

Painless Killing of Crabs and Other Large Crustaceans

Abstract. Large crustaceans used for food are customarily scalded to death. This is unnecessary torture, for it can be avoided easily. It is possible to kill the animals quickly, without pain, by placing them in cool fresh water and raising the temperature steadily to about 40°C.

The ability to feel pain and avoid it is probably an absolute necessity for motile organisms, but where pain cannot be avoided it is useless, and to inflict it only results in the torture of helpless creatures, whatever the circumstance. Predatory animals quite generally inflict pain in the process of getting food, and C. S. Sherrington pointed out some years ago that life existed for eons on the earth without the manifestation of pity or compassion, until the relatively recent advent of the human mind. Attitudes of kindness are not uniformly present in the human race, but probably the more civilized components of this group agree with the zoologist W. K. Brooks (1), who said, "As for myself, I try to treat all living things, plants as well as animals, as if they may have some small part of a sensitive life like my own. . . ." Thus, there is some tendency for civilized man to avoid inflicting unnecessary pain upon lower animals. Recent laws concerned with the painless killing of cattle in slaughterhouses are a case in point. However, these laws, and public sympathy, largely apply to mammals, and the invertebrate animals are given very little consideration, as yet.

The more hardy crustaceans, such as several kinds of crabs, lobsters, spiny lobsters, and the like, are generally taken alive and sold alive, because the consumer has come to believe that a dead crab or lobster is a spoiled one. The assumption is not always justified, but it is a good rule of thumb, and its widespread application has prevented a great deal of food poisoning. Because of the fact that a live crustacean is the only accepted guarantee of an unspoiled one, these animals are killed at the time of cooking. In the home the prevalent custom is to scald the crabs to death in boiling water. Commercial packers and canners make use of live steam for the same purpose. Some people think nothing of this because the victims are lower animals, and others excuse themselves on the grounds that the process only lasts a few seconds. However, anyone who watches the violent reactions of crabs being scalded to death can see that they suffer extreme pain, and fishery marketing agents have pointed out that thousands of American housewives will not cook fresh lobsters or crabs because of that fact.

The purpose of this report is to describe an easy and painless way to kill large crustaceans, which depends upon the simple fact that most aquatic organisms can withstand very little heat. Marine organisms, especially those in tropical and warm temperate regions, live in their natural environment much closer to the lethal limit of heat than to the lethal limit of cold. Most tropical marine invertebrates cannot survive when water temperatures rise above 37°C, and nearly all of them are killed by the equivalent of mammalian blood heat. (These remarks do not apply to intertidal animals.) Crustaceans from colder climes may even be killed by temperatures of 30°C. Further details are given in the "Treatise on Marine Ecology and Paleoecology" (*2*).

Some people try to kill crabs by placing them in fresh water. This is not effective with euryhaline organisms, such as the blue crab, which sometimes invade fresh water (*3*). However, fresh water has some anesthetizing effect because it leaches salt from the body fluids. Only one more thing is needed for painless killing of crabs and that is a low flame under the pot, which slowly raises the water temperature to about 40°C. Crustaceans subjected to this treatment die quickly and easily without showing distress. The water feels only lukewarm to the hand, and the dead crabs or lobsters are perfectly limp because death from heat occurs long before coagulation of the protein, which takes place at about 70°C (*4*). Occasionally, a crab in the bottom of the pot, where his legs are in direct contact with the metal, will stir about because he feels the heat. This can be prevented by using a small wire or metal lattice to keep the animals on the bottom from direct contact with the vessel.

I have demonstrated this little experiment several times, but the facts deserve wider publicity because they may lead to some lessening of the practice of inflicting unnecessary pain. There is a false idea in some quarters that crabs are not good unless they are scalded to death suddenly. With the procedure described above, as soon as the crustaceans are dead, the heat can be turned up and the water boiled quickly; the meat of crabs treated in this manner is just as good as that of animals killed by scalding.

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1. W. K. Brooks, *The Foundations of Zoology* (Columbia Univ. Press, New York, 1907), p. 17.
2. G. Gunter, *Geol. Soc. Am. Mem. No. 67* (1951), vol. 1, chap. 8.
3. ———, *Science* **87**, 87 (1938).
4. L. V. Heilbrunn, *Am. J. Physiol.* **69**, 190 (1924).

3 October 1960

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].

Depression of Taste Sensitivity to Specific Sugars by Their Presence during Development

Abstract. A chemoreceptor neuron of the adult blowfly contains several different sites for activation by sugars. It appears that the number or affinity of the sites for fructose and perhaps those for glucose may be depressed by rearing the larvae in the presence of the sugar in question.

The labellar and tarsal chemosensory hairs of the blowfly (*Phormia regina* Meig.) contain two neurons that respond to chemical stimulation (*1*). The input of one of these, the *S* fiber, is responsible for the behavioral modality "acceptable" and is evoked by a highly specific group of polyols, especially sugars (*1–3*). Behavioral studies of the effectiveness of sugar mixtures sug-

Table 1. Relative sensitivity of adult flies to sugars as affected by sugars in the larval medium (0.1*M*). Individual ascending tarsal thresholds to the sugars were obtained (molar units), and n was calculated from the following formula: glucose threshold = fructose (or sucrose) threshold $\times 2^n$.

Larval medium	$\bar{n} \pm$ S.E.	*t* Test with controls		Tests (No.)	$\bar{n}$ 2	Mean threshold		
		t	*P*			Glucose	Fructose	Sucrose
Control	+ 4.70 ± 0.07			251	26.1	0.76	0.032	
Mannose	+ 4.74 ± 0.11	0.3	>0.7	114	26.7	0.70	0.036	
Glucose	+ 5.21 ± 0.35	4.0	<0.001	273	37.0	0.69	0.026	
Fructose	− 0.52 ± 0.10	43	<0.001	120	0.73	1.34	1.46	
Control	+ 3.50 ± 0.058			251	11.3	0.76		0.078
Glucose	+ 4.77 ± 0.066	14.5	<0.001	273	27.4	0.69		0.034
Fructose	+ 1.67 ± 0.080	12.9	<0.001	138	3.2	1.18		0.65

gested that there must be more than one type of receptor site on this neuron, each with its own structural requirements for effective combination. Glucose and fructose, for example, appear to act at independent sites (*3, 4*). Even more effectively, one can argue on the basis of configurational and conformational analysis that a single site cannot account for the effectiveness of all the polyols that have been tested (*3*). Such a specific system with apparent adaptive significance would be expected to be under genetic control and susceptible to environmental influences during development. An example of the latter, "olfactory conditioning," has long been known in insects (*5*) but remains essentially unanalyzed. The presence of an odorous compound during larval life can make that compound attractive to the subsequent adult even though that chemical normally would be repellent or would lack adaptive significance, and in spite of the intervention of a complete metamorphosis. Homing by the adult salmon also seems to involve orientation to chemicals that were present during development (*6*).

On the basis of these considerations, we have assessed the effect on the taste sensitivity of adult flies of rearing them as larvae on media containing glucose, fructose, or mannose. The usual medium (*7*), composed of dried yeast and milk, agar, and water served as the control. To it in the three experimental groups was added 0.1*M* glucose, fructose, or mannose; in these cases it was necessary to reduce the agar concentration by one-fourth to retain the requisite physical properties. The adults that emerged were tested, behaviorally, on sugar solutions between 3 and 6 days after eclosion, by the method of Evans and L. Barton Browne (*8*). This method measures the minimal concentration of each of two sugars that will elicit proboscis extension when applied to the tarsal taste receptors. The results are then expressed as the relative sensitivity to the two sugars, since the absolute sensitivity varies greatly with feeding and starvation (*9*). Accordingly, the ascending thresholds for glucose and fructose (or sucrose) were determined for each fly; the results (Table 1) were then expressed and analyzed in terms of n in the following formula:

$$\text{Fructose threshold} \times 2^n = \text{glucose threshold}$$

For the controls and mannose-reared flies, fructose was about 26 times more stimulating than glucose [23 is the value obtained by Hassett *et al.* (*10*) under the same conditions as those of our controls]. This value was elevated to 37 in the glucose-reared and depressed to less than unity in the fructose-reared flies; both of these values were highly significant. Also given in the table is the average threshold for each sugar. In the fructose-reared flies the change in relative sensitivity is plainly due to a great decrease in sensitivity to fructose.

The behavioral testing method leaves much to be desired, but there is as yet no reliable electrophysiological method suitable for obtaining quantitative data. Nonetheless, the results permit a few unequivocal conclusions. Rearing on fructose markedly altered the relative sensitivity to the two sugars, primarily by greatly decreasing the sensitivity to fructose. Rearing on glucose had less effect, but, significantly, altered the relative sensitivity in the opposite direction; the data do not permit a decision as to whether or not this was due to a decrease in sensitivity to glucose. The influence on sucrose sensitivity of media fed the larvae (Table 1) paralleled the influence on fructose sensitivity; sucrose acts predominantly at the fructose site (*3*). The mannose medium was without effect; this sugar normally is very weakly stimulating [the extrapolated 50-percent acceptance threshold is 7.6*M* (*10*)]. The mannose-reared flies were repeatedly tested on mannose solutions, but no response was obtained even to saturated solutions.

Upon analysis it was found that the normal medium contains approximately 0.1*M* lactose and no appreciable amount of any other mono- or oligosaccharide; lactose is tasteless to flies grown on this medium (*10*). As was later realized and is now being practiced, *Phormia* larvae can readily be grown on a chemically defined, sterile medium that does not contain any carbohydrate; casein is the only constituent present at macronutrient levels (*11*). And we have found that sugars may be added to the medium without detriment at the concentrations used in the experiments reported above. The experiments are being repeated with this improved medium.

We are attracted to the hypothesis that the effective sugars act by depressing sensitivity specifically to themselves and to other sugars that act at the same site, and that this is due to a decrease in the number of affinity of their combining sites on the sugar-sensitive neuron. While this is purely hypothetical, one may realistically expect to be able soon to make a direct test by electrophysiological methods.

As for possible mechanisms for the depressive effect obtained, recent progress in the study of "regulator" genes suggests a possible model. In *Escherichia coli*, tryptophan leads to repression of the formation of the sequence of enzymes responsible for its synthesis (*12*). Recent attempts to apply the concepts of biochemical genetics to immune tolerance and development (*13*) predict the direction of the result obtained in the case reported here under certain assumed conditions. The gene product here would be, in all probability, a specific receptor site associated with the cell surface (like "permease"), the function of which was the transduction of chemical into electrical potential (*14*).

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Pliable, Root-Permeable Layers for Separation of Portions of Experimental Plant Root Systems

Abstract. A description is given of simply made, sturdy, pliable layers which may be placed in rooting media for studies of divided root systems. Roots readily penetrate the layers but form a tight seal in doing so. The layer remains impermeable to water and ions.

In the study of plants under controlled conditions it is often necessary to separate portions of the root system of a growing plant by special layers in the root medium in order to confine ions, water, and microorganisms to the desired regions. In such instances it is frequently desirable to fabricate the layers from materials impermeable to ions, water, and microorganisms but readily penetrable by roots. Such materials have been reported (*1*). Some materials have been cumbersome and have had to be formed in place when needed. Thin layers are desirable but have not always been attained. This report describes a material which possesses required impermeability and which can be penetrated by roots; furthermore, it possesses strength and simplicity of design and forms layers which are reasonably thin.

The layers are composed of a 1:1 mixture (by weight) of paraffin wax and rosin. The substance is prepared by melting and mixing the two components in a common container. When the mixture has reached the boiling point, a quantity (75 to 80 ml, for example) of the liquid is poured on the surface of water which has been heated to 60°C. The water, ½ in. deep, is contained in a shallow pan (a pan 12 in. in diameter and 1½ in. deep has sufficed for this purpose). Water of this depth seems to exhibit a stability of surface desirable for preparation of the layers. The poured mixture is allowed to cool until firm.

The material, prepared according to these specifications of quantity of mixture, temperature, and size of pan, produces a layer about 11 in. in diameter and about 1 mm thick. The layer is of rather uniform thickness throughout, thinning out somewhat at the very edge. The thickness obtained is primarily a function of the initial temperature of the water: lower temperatures produce thicker layers. The best results were obtained by pouring the melt down a glass rod which was in contact with the water at one end. This eliminated the formation of bubbles in the layer. What temperature produces a layer of a given thickness depends upon the composition of the paraffin and rosin and is best determined by experimentation.

The cooled layer can be removed from the pan by hand, molded, cut, handled, and pressed into shape to conform to a vessel, then sealed into place with a piece of heated metal or ceramic. A soldering iron has sufficed for this purpose. If the material is accidentally torn, repair by the same procedures is possible. When used in a pot experiment, the material showed no evidence of decomposition over a 3-month period. It appeared to have no toxic or inhibitory effect on the roots of either white clover (*Trifolium repens* L.) or common Bermuda grass (*Cynodon dactylon* L.).

The material appears to be impermeable to ions. In a study in which radioisotopes of strontium were used, no movement of the ions through layers of the wax material was observed. The material is impermeable to water. It appears, further, that a tight seal exists between the material and a root which has penetrated the layer. Penetration of roots has not produced measurable movement of water or ions past the layer.

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Effect of Mitomycin C on Lateral Root-Tip Chromosomes of Vicia faba

Abstract. Lateral root-tip chromosomes of *Vicia faba* were treated with mitomycin C. Chromatid aberrations were observed from 24 through 96 hours after treatment. The effect of mitomycin C was not altered appreciably by changes in *p*H, temperature, oxygen tension, or lack of adenosine triphosphate. The relationship of mitomycin C to other radiomimetic compounds is discussed.

In two recent papers Sekiguchi and Takagi (*1*, *2*) demonstrated two remarkable effects of mitocycin C. They showed an inhibition of deoxyribonucleic acid synthesis by phage-infected *Escherichia coli* in the presence of mitomycin C (*1*) and the production of what the authors termed "abnormal DNA" by bacteriophages infecting *E. coli* in the presence of a high level of mitomycin C (*2*). Sekiguchi and Takagi also observed that, although DNA synthesis was inhibited in *E. coli* during treatment with mitomycin C, there was

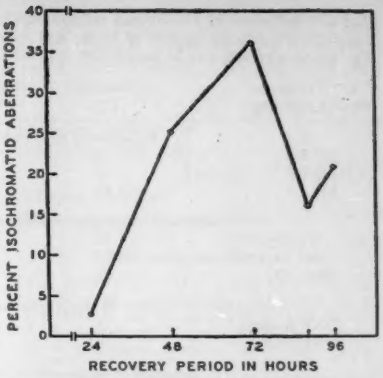

Fig. 1. Frequencies of isochromatid aberrations obtained at different fixation times after treatment.

no such inhibition of protein or ribonucleic acid synthesis (*1*). It seemed, then, that mitomycin C would be an excellent agent to use in determining whether the "rejoining system" would be inhibited in the absence of DNA synthesis, as it has been shown to be in the absence of protein synthesis (*3*). During tests to determine whether rejoining was in fact inhibited by mitomycin C, chromosomal aberrations were observed in root-tip cells treated with the agent alone. This is a report of the ensuing study of mitomycin C as a member of a rapidly increasing list of interesting radiomimetic compounds.

The material used in the experiments consisted of lateral root tips of the broad bean, *Vicia faba* (*4*). As has been previously described (*5*), the roots were grown in shell vials in the dark at 25°C for 7 days after an initial 24-hour period of soaking. The tap water was changed daily during growth and recovery (the latter being the time interval between treatment and fixation). Twenty-four hours before treatment the roots were placed in an incubator at 17°C. Treatments were carried out at 20°C, unless otherwise stated, and recovery took place at 17°C in the dark. The root tips were treated with 0.05-percent colchicine for 3 to 4 hours before fixation in cold alcohol and acetic acid (3:1), and slides were prepared as Feulgen squashes. The treatments were carried out in shell vials. The method for the introduction of gases has been described previously (*6*). Pretreatment with dinitrophenol (DNP) for 2 hours was carried out to test the effect of energy deprivation on the mitomycin C effect (*7*).

Various concentrations of mitomycin C were tried. It was found that concentrations of 0.1 percent, 0.01 percent for 1 hour, and 0.001 percent for 2 hours were lethal, death of cells ocur-

Table 1. Influence of *p*H, oxygen tension, dinitrophenol (DNP), and temperature on the effect of mitomycin C on root-tip cells of *Vicia faba*. All roots were treated with 0.001 percent mitomycin C; the recovery period was 72 hours; 200 cells were scored for each treatment.

Treatment conditions	Normal (%)	Abnormal (%)	Deletions (%)	Isochromatids (%)	Exchanges (%)
Influence of pH; roots treated at 20°C in air					
*p*H 8.5	70	30	0	32	21
*p*H 6.8	66	34	0	36	17
*p*H 4.5	62	38	0	55	15
Influence of oxygen tension; roots treated at pH 6.8 at 20°C					
0% O_2 (N_2)	54	46	0	39	21
20% O_2 (air)	55	45	0	56	16
100% O_2	58	42	0	44	19
Influence of 1×10^{-4} M dinitrophenol; roots treated at pH 6.8 at 20°C in air					
DNP present	55	45	0	58	16
DNP absent	58	42	0	36	16
Influence of temperature; roots treated at pH 6.8 in air					
Temp. 10°C	52	48	0	61	15
Temp. 25°C	55	45	0	56	16

ring within 48 hours. A concentration of 0.0005 percent for 1 hour produced no lethal effect, some inhibition of mitosis (few division figures were apparent 24 hours after treatment), and a low frequency of chromatid aberrations 48 and 72 hours after treatment. A 0.001-percent concentration of mitomycin C with a 1-hour treatment period proved to be the most efficient combination for examining the effect of this compound on chromosomes. After treatment with 0.001-percent mitomycin C there was a marked inhibition of mitosis. Few division figures or aberrations occurred 24 hours after treatment. The graph (Fig. 1) illustrates the frequencies of isochromatid aberrations obtained at different fixation times after treatment. The highest frequency was obtained at 72 hours and the frequency decreased thereafter, but the level of isochromatid aberrations was still high 96 hours after treatment. It would be very difficult to determine the mitotic stage that is most sensitive to mitomycin C, since mitotis is inhibited to such an extent after treatment. The highest frequency of aberrations coincided with the highest frequency of division (at 72 hours), but the rate was maintained at a constantly high level from 48 through 96 hours. These data suggest that at least most interphase stages are sensitive to mitomycin C.

Since many of the chemical mutagens produce different results in different environments, it was of interest to determine how such alterations of the environment as *p*H changes, variations in oxygen tension, elimination of adenosine triphosphate, and changes in temperature altered the effect of mitomycin C. The results of experiments designed to determine the nature of the influence of these environmental changes on the effects of mitomycin C are listed in Table 1. The results seem to indicate that varying the environment during treatment with mitomycin C does not appreciably alter the ability of this mutagen to induce breaks.

Another interesting property of many radiomimetic compounds is their ability to produce breaks in one or more specific areas along the lengths of the chromosomes of *Vicia faba*. In contrast to breaks induced by x-rays, which seem to be distributed more or less at random (*8*), breaks induced by 8-ethoxycaffeine are concentrated in the nucleolar constriction (*6, 9*), those induced by maleic hydrazide occur in segments of heterochromatin on either side of the centromere of the long chromosome, and breaks induced by beta-propiolactone, nitrogen mustard, di(2,3-epoxypropyl) ether, and potassium cyanide occur in heterochromatic segments in the middle of the short chromosomes (*8, 10, 11*). Also, when breaks are distributed in somewhat random fashion, the rates obtained by dividing the total number of breaks in the short chromosomes by the total number of breaks in the long chromosomes (*S/L* ratio) is approximately 2.5 (*11*). The *S/L* ratios observed after treatment with 8-ethoxycaffeine or maleic hydrazide are less than 1 (*11*), whereas those observed after treatment with nitrogen mustard or di-epoxide are greater than 2.5 (*11*).

Over 800 breaks (in 450 cells) induced by mitomycin C were scored as to location. The *S/L* ratio was observed to be about 1.5, indicating some specificity for the long chromosomes. Approximately 80 percent of the breaks observed in the long chromosomes were situated in the nucleolar organizer constriction, about 15 percent being located in the heterochromatic segments on either side of the centromere. Most of the other breaks occurred in the heterochromatic segments of the short chromosomes. In all, about 93 percent of the breaks were located in heterochromatin.

Mitomycin C, like most radiomimetic compounds, has unique qualities. For example, like beta-propiolactone, nitrogen mustard, di-epoxide, and several others, it seems to act independently of oxygen tension, temperature, and *p*H; but the breaks induced are mainly concentrated in the long chromosomes as are those induced by 8-ethoxycaffeine and maleic hydrazide, which, however, are known to exhibit a strong oxygen and temperature dependency.

Because mitomycin C is of interest as a carcinostat, it is desirable to know whether its anticarcinogenic characteristics can be maintained through its action on DNA synthesis at the same time that its capacity to break chromosomes is inhibited; conceivably, its inherent toxicity to human beings would be reduced by such inhibitions. It is of interest, therefore, to know to what degree its action on DNA synthesis is related to its ability to break chromosomes, and to what degree both properties are related to its action as an anticarcinogen (*12*).

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Sensory Deprivation and Pain Thresholds

Abstract. Four days of sensory deprivation produced a significant lowering of thresholds for electrically induced pain.

Eighteen male adult subjects served in a study to determine the effects of sensory deprivation upon cutaneous pain thresholds (*1*). Each subject spent a minimum of 1 hour per day in the deprivation chamber, during which time pain thresholds were measured. These periods were considered to be practice periods. Most subjects served in this manner for 3 or 4 days before their thresholds became sufficiently stable to

Table 1. Mean pain thresholds (in milliamperes).

Test No.	Sensory deprivation group	Control group
1	0.290	0.240
2	0.182	0.221
Difference	0.108	0.019

be considered reliable. The criterion of reliability was taken to be variability of less than 10 percent for an entire practice period. If a subject did not meet this criterion in the course of four practice periods he was eliminated from the study. The practice periods were discontinued at the conclusion of the period in which the criterion was met.

The sensation of pain was elicited by applying an electrical current of a frequency of 1000 cy/sec through small dry electrodes clamped to either side of the lobe of the right ear. The electrodes were brass disks, 7 mm in diameter, which were firmly clamped to the ear lobe but caused no discomfort. The weight of the electrodes, of the clamping device, and of the connecting wires was supported in such a manner that there was no sensation of weight or pull at the ear. The stimulus, which originated from an oscillator, was amplified by a constant-current amplifier. The intensity of the stimulus delivered to the subject was controlled by an attenuator. The wave was constantly monitored by an oscilloscope to see that it was sinusoidal.

Pain thresholds were determined by a modified method of limits, the 50-percent value being calculated. The method of limits was modified so that stimuli of an intensity very much in excess of threshold were not used. High-intensity stimuli of this nature are not only extremely unpleasant for the subject but they also produce such a persistent aftereffect that they mask subsequent stimuli. Even a stimulus of threshold intensity produced what was characteristically described as "stinging, nasty pain."

On the day after the last practice period, each subject was brought back for an additional session, when his pain threshold was determined. This usually required about 100 presentations of the electrical stimuli.

After the pain threshold had been determined, nine of the subjects were exposed, one at a time, to 4 days of sensory deprivation. A detailed description of the conditions of the confinement can be found in Vernon *et al.* (*2*). For the present, it is sufficient to say that sensory deprivation consisted of confinement in a small lightproof and soundproof cubicle. The cubicle was barely large enough to contain a single bed, upon which the subject lay. At the end of the 4 days of confinement and before he left the deprivation chamber, the subject's pain threshold was determined a second time.

The remaining nine subjects were not exposed to sensory deprivation, and thus they provided a control group. Four days after their pain thresholds had been determined they were called back to the laboratory, where a second determination of their pain thresholds was made. The pain thresholds for all subjects were determined in the sensory deprivation chamber under identical conditions. The major difference between the two groups was the manner in which they spent the 4 days which intervened between the first and second determinations of their pain thresholds. The experimental group spent this period under conditions of sensory deprivation, while the control group spent it in the normal manner.

The data for these two groups, presented in Table 1, reveal that, on the average, the pain threshold for the confined group dropped 0.108 ma after 96 hours of sensory deprivation. This change is statistically significant at better than the 1-percent level of confidence (*3*). All the experimental subjects showed a lowered pain threshold on the second determination. The control group showed a slight drop in pain threshold which averaged 0.019 ma—a change that is not significant. About half of the control group showed a rise in threshold, the other half, a drop. Thus, it can be seen that sensory deprivation not only has a uniform effect upon pain thresholds but also produces an increase in sensitivity. This is not the first instance of an increase in sensitivity resulting from isolation. Doane *et al.* (*4*) found the two-point limen to be significantly lowered after 48 and 72 hours of confinement.

One explanation of this finding is that a contrast phenomenon is produced by sensory deprivation. Another and more involved explanation can be formulated in terms of the action of the reticular formation of the brain stem. Under normal circumstances neural inputs from sensory departments can be blocked or partially inhibited at the level of the reticular formation. The blocking is produced in the descending tracts under cortical excitation aroused by any sensory stimulation. Thus it may be that sensory deprivation, by drastically reducing the amount of sensory input, minimizes the activity in the descending tracts of the reticular formation. If there is less inhibition to overcome at that level, then perhaps sensitivity is accordingly increased. In the case of pain, the neural impulses resulting from the pain stimuli would encounter less opposition and would register at a lower level of intensity. Or, to state it more accurately, registration would occur with impulses of lower frequency.

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Selective Viral and Rickettsial Serum Antibody Absorption by a Chromatographic Column

Abstract. Serum antibodies behave as cations at neutral *p*H and thus have low affinity for cellulose anion-exchange columns. Antigens of small size derived from adenovirus, influenza virus, and typhus rickettsiae, however, readily adsorbed to such columns. These adsorbed antigens specifically removed antibodies from antisera. This simple method permits antibody absorption by antigens ordinarily sedimented with difficulty.

Absorption of serum antibodies with particulate antigens has been a useful approach to the analysis of antigenic structure and antibody populations. This report presents a new method for antibody absorption which employs a chromatographic column to which "soluble antigens" are attached (adsorbed). Chromatographic columns, binding antigens covalently to resins or nonspecifically to other substances, have been employed to absorb and purify antibodies (*1*). Difficulties associated with this use of columns have been nonspecific antibody adherence to columns, antigen damage during chemical manipulations, and impair-

Table 1. Adenovirus type 7 serum (human, convalescent) before and after absorption by column antigens.

Column antigen	Serum CF titer with antigens*		
	Type 3	Type 4	Type 7
None	40	40	40
Adenovirus, type 7	<10	<10	<10
Adenovirus, type 4	<10	<10	<10

* Figures represent the reciprocal of the highest dilution of serum-fixing complement in the presence of four units of antigen.

Table 2. Influenza serum (human) before and after absorption by column antigens.

Column antigen	Serum CF titer with antigens*		Serum HAI titer with antigens†	
	A'/Hawaii/303/56	A2/Jap/305/57	A'	A2
None	80	80	80	10
A'/Hawaii/303/56	<10	<10	<5	<5
A2/Jap/305/57	<10	<10	80	<5

* Reciprocal of the highest dilution of serum-fixing complement in the presence of four units of antigen.
† Reciprocal of the highest dilution of serum inhibiting four hemagglutinating units of virus.

ment of flow in columns. The usual cationic character of serum antibodies at neutral *p*H contrasts with the anionic nature of many proteins at this *p*H. The anion-exchange capacity of ECTEOLA cellulose (*2*) was employed in the study reported here, to allow attachment of several antigens but not attachment of antibodies.

Antigens were prepared from three groups of organisms: adenoviruses from frozen and thawed infected HeLa cells and tissue-culture fluid; influenza virus from ether-treated (*3*), infected raw chick-embryo allantoic fluid; and typhus group rickettsiae from infected yolk sacs, ether-treated by method No. 3 of Topping and Shepard (*4*). These antigens were placed on columns of ECTEOLA cellulose, capacity about 0.3 meq/g, in 0.005*M* potassium phosphate buffer (*p*H 7.2), at room temperature, by the method of Hoyer *et al.* (*5*). Complement fixation (CF) tests with appropriate guinea pig or human antisera on each effluent indicated no antigen—that is, full antigen adsorption. Furthermore, there was no hemagglutinating antigen in the effluents from columns exposed to influenza antigens. After the column had been washed with the same buffer, an aliquot of human or guinea pig antiserum, dialyzed to the same conditions, was passed over the antigen-loaded column. The effluent was concentrated to the original serum volume by dialysis against polyethylene glycol (*6*) and assayed for antibody content with standard complement-fixation, neutralization (NT), or hemagglutination-inhibition (HAI) procedures. For complement-fixation and hemagglutination-inhibition tests, antigens were prepared as described above. For the typhus neutralization determinations, yolk-sac suspensions of viable *Rickettsia prowazeki* and *R. mooseri* were employed.

Table 3. Epidemic typhus serum (guinea pig, convalescent) before and after absorption by column antigens.

Column antigen	Serum CF titer with antigens*		Serum NT titer with toxic suspensions†	
	Epidemic	Murine	Epidemic	Murine
None	160	40	128	8
Epidemic	<10	<10	8	4
Murine	80	<10	112	<2.5

* Reciprocal of the highest dilution of serum-fixing complement in the presence of four units of antigen.
† Reciprocal of theoretical dilution of serum protecting two of four mice from 2 LD_{50} of toxic suspension, interpolated by the method of Reed and Muench.

Typical results are shown in Tables 1–3. It may be noted that adenovirus complement-fixation antibody to three types was removed by either a homologous or a heterologous type antigen (Table 1). Similarly effective was the absorption of complement-fixation antibody from a human serum by two type-A influenza strains (Table 2). Hemagglutination-inhibition antibodies were removed more selectively by the A2 than by the A' antigen, but the low initial A2–hemagglutination-inhibition titer makes interpretation difficult. Epidemic typhus antiserum lost essentially all complement-fixation and neutralization antibody after homologous absorption, while heterologous absorption reduced predominantly the heterologous antibody (Table 3).

Certain additional reciprocal cross-absorption experiments have been performed, with similar results. The typhus system has been the most fully studied. Characterization of the type-specific adenovirus antibodies was not possible with the sera studied because, following the preabsorption dialysis, no type-specific antibody was detectable in these sera. The specificity of absorption of influenza hemagglutination-inhibition antibody requires further study. Storage of certain antigen-loaded columns, at 4°C, between repeated absorptions for periods up to 2 months did not impair their absorbing ability. This observation suggests that Formalin treatment of antigens (*7*) may allow not only additional useful storage but also column adsorption of other antigens with less initial affinity for anion-exchange materials.

The most obvious interpretation of these data seems to be that antibody combined with column-bound antigen which remained *in situ*. The possibility that antibody, once united with antigen, eluted in a serologically inactive form cannot be excluded, particularly from the hemagglutination-inhibition and neutralization data. However, antigen-antibody complexes in serum usually fix complement alone and are thus discerned as "anticomplementary sera." Anticomplementary sera were not encountered with this system except when DEAE cellulose (*2*), of 0.93 meq/g capacity, was employed under identical conditions.

This absorption method, in which soluble antigens attached to cationic particulates are used, may provide a sensitive tool for the differentiation of virus strains and for quantitative studies of antibody response after infection. More diverse application of this methodology to other antigen-antibody systems is suggested by the considerable number of proteins and microorganisms adsorbable to the cellulose anion exchangers.

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* Present address: University of Washington School of Medicine, King County Hospital, Seattle.

18 August 1960

A "D"-like Antigen in Rhesus Red Blood Cells and in Rh-Positive and Rh-Negative Red Cells

Abstract. A "D"-like antigen has been demonstrated in human and rhesus red cells. These red cells, as well as heat extracts of human blood (Rh-positive or Rh-negative), induce formation of "D"-like antibodies in guinea pigs. These antibodies, when exposed to rhesus red cells or to Rh-positive or Rh-negative red cells, yield eluates of "D"-like specificity.

The unexpected findings of Murray (*1*) and Murray and Clark (*2*) that heat extracts of Rh-positive or -negative red cells, when injected into guinea pigs, produce an antibody which they believe showed anti-D specificity have been confirmed. Red cells washed three times were suspended in an equal volume of saline and heated at 50°C for 20 minutes. The red cells were removed by centrifugation at 1500 *g* for 10 minutes. Guinea pigs were injected intraperitoneally twice with 5 ml of the heated extracts at an interval of 3 days and tested 10 days later.

In two different series we injected 12 guinea pigs with extracts of D--/D-- red cells containing an excess of D

Table 1. Ready production of the "D"-like antibody.

Injection	Number	
	"D"-like antibody produced	No antigenic response
Heat extracts of Rh-negative red blood cells (rbc)	13	7
Heat extracts of Rh-positive (R_2r) rbc	4	4
Heat extracts of Rh-positive (D-- /D--) rbc	6	6
Rh-positive (R_2R_2) rbc	7	2
Washed sediments from heat extracts of Rh-positive rbc	6	4
Washed sediments from heat extracts of Rh-negative rbc	5	5

antigen, and 6 out of 12 produced anti-D-like specificity, but only one gave strong reactions. Of the 20 animals injected with heat extracts of Rh-negative blood, 13 produced good to moderate effects. In all cases the sera were absorbed with Rh-negative blood in dilutions of 1:5 or 1:10 and tested with red cells suspended in saline.

Ponder and Ponder (*3*) had shown that the heat extracts when ultracentrifuged yielded a sediment consisting of tiny fragments and "myelin" forms released from the red cells by heating. These were readily visible by phase microscopy. Subsequently, Murray and Clark (*2*) demonstrated that guinea pigs, when injected with the washed sediment derived from heat extracts of Rh-negative blood and centrifuged at 10,000 rev/min, produced an antibody which they believed showed anti-D specificity. This observation was confirmed in our experiments with the heat extracts of Rh-positive blood, sedimented at 30,000 *g* and washed three times at the same or higher centrifugal fields. Of ten animals, each injected twice with the sediment derived from the heat extracts of a total of 20 ml of whole blood, six produced good antibody response. In similar experiments with the sedimented particles from heat extracts of Rh-negative blood, five out of ten guinea pigs produced the antibody.

The production in guinea pigs of an antibody with "D"-like specificity upon injection of Rh-positive, Rh-negative, or rhesus red cells was demonstrated.

Table 1 records the results of injecting (*4*) guinea pigs with heat extracts (50°C) of Rh-negative red cells, heat extracts of two series of Rh-positive red cells, one series with Rh-positive red blood cells (R_2R_2), the washed sediment from heat extracts of Rh-positive blood, and also from Rh-negative blood. In each of these series there is a high incidence of production of the "D"-like antibody.

The relation of the "D"-like antigen in Rh-positive and Rh-negative red cells or their extracts and in rhesus red cells to the usual D antigen of Rh-positive blood requires extensive study. Thus far, the "D"-like antibodies produced in guinea pigs seem to differ from human anti-D in several respects, among which the following are cited: (i) Rh-positive red cells blocked with a powerful blocking anti-D [or selected cells sensitized with anti-c (hr')] are still agglutinated by the "D"-like antibody produced in guinea pigs injected with rhesus red cells or heat extracts of Rh-positive or Rh-negative blood. (ii) The "D"-like antibodies induced by any material containing the "D"-like antigen when exposed to Rh-positive, Rh-negative, or rhesus red cells yield eluates showing "D"-like specificity, while Rh-negative red cells, possessing as they do the "D"-like antigen, when exposed to human anti-D do not yield active eluates.

No antibody to the "D"-like antigen is obtained if the heat extracts are prepared from either trypsinized Rh-positive or Rh-negative red cells (*5*).

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4. The technical assistance of Thomas J. Pluhar is acknowledged.
5. A fuller discussion of these findings is in preparation.

14 November 1960

Effect of Strychnine upon the Electrical Activity of an Isolated Nerve Cell

Abstract. The effect of strychnine upon the electrical activity recorded from the axon and the soma of an isolated nerve cell (the nonadapting stretch receptor cell of the crayfish) was studied. Protracted exposure of the soma of the cell to strychnine prolongs the duration of the intracellulary recorded action potential, as has been described in other excitable tissues treated with quaternary ammonium ions. During the plateau in the falling phase of the soma spike, the axon is usually firing repetitively. The stimulation of the inhibitory fiber produces a premature termination of the prolonged spike.

The effects of strychnine upon the activity of a single nerve fiber are known (*1*). Strychnine has also been extensively used in electrophysiological investigations of central nervous system activities. In these experiments, however, the inferences which can be drawn concerning the actions of the compound are limited because of the complex structural and functional arrangements in the central nervous system. We have not seen in the literature a study of the effect of strychnine upon the electrical activity of a single, isolated nerve cell.

The stretch receptor of Crustacea (*2*), which has been studied physiologically by several investigators (*3*, *4*), is a suitable preparation for such a study. The soma of the isolated nerve cell can be easily penetrated by microelectrodes, and both excitatory (the generator potential set up by stretch) and inhibitory stimulation may be applied.

Nonadapting abdominal stretch receptors of crayfish were dissected and mounted on a device similar to that described by Eyzaguirre and Kuffler (*4*). The fast-adapting receptor was cut off. The preparation was suspended in a plastic box containing Van Harreveld solution. The axon was raised into a layer of mineral oil where platinum electrodes recorded the discharge. Micropipets filled with potassium chloride were used to penetrate the cell; they were mounted in a bridge circuit permitting simultaneous recording and stimulation. After the addition of a strychnine sulfate solution (1 percent) to the perfusion fluid (final concentration about 0.03 percent), the exceedingly regular discharge of the receptor to a steady stretch was broken and bursts of spikes were recorded from the axon, which were followed by pauses.

The cell must be depolarized, either by stretch or by application of a pulse of cathodal current through the impaling microelectrode, for the strychnine type of activity to appear. The threshold to direct stimulation was not altered appreciably, but a short burst of spikes (two or three) was initiated at a rheobasic current. The membrane resistance and the resting potential were not altered. The frequency of occurrence of the bursts increased with increasing degree of stretch, while the number of spikes in the bursts decreased. A total desynchronization with a return to the regular discharge of the receptor could be obtained if a high degree of stretch was applied or if calcium ions were added to the solution.

The changes described are due to the action exerted by strychnine mostly upon the membrane of the cell (and possibly the initial portion of the axon) rather than upon the axonal membrane (at the concentration used). When the muscle bundle and the soma of the cell were kept in oil, with only several millimeters of the axon being lowered in

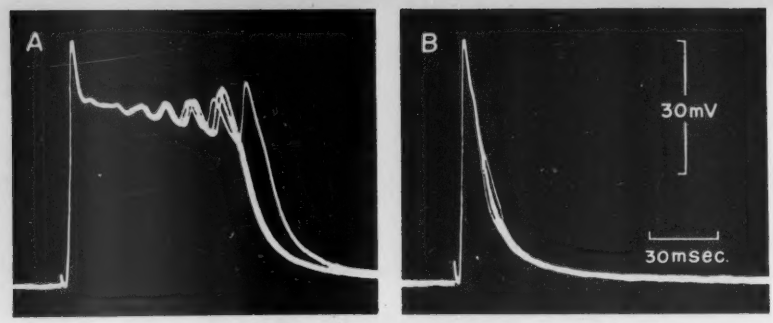

Fig. 1. (*A* and *B*) Superimposed action potentials evoked by antidromic stimulation. In *B*, inhibitory fiber stimulation caused a premature termination of the prolonged action potential.

the saline containing strychnine before being raised again into the oil layer, no alteration of activity took place. When the cell was lowered into the saline, the changes in activity described soon appeared.

After 5 to 10 minutes of exposure to strychnine, only long bursts of spikes (from five to 20 or more) were recorded from the axon except at extreme degrees of stretch. Intracellular recording from the soma in this condition showed: (i) no effect of strychnine on the membrane potential—the membrane's resistance was not changed; (ii) a prolongation of spike potential by a plateau which developed during the falling phase of the spike and which could be as long as several seconds; (iii) a series of oscillations during the plateau. The amplitude of these oscillations increased toward the end of the plateau.

A premature termination of the prolonged spike potential was obtained by applying a short pulse of inward current during the plateau. The phenomenon was all-or-none in nature. Refractoriness was present after a prolonged action potential; this finding resulted when a second action potential was induced at different time intervals by direct or antidromic stimulation. The characteristics described are similar to those of the action potential recorded from cardiac muscle fibers (*5*), crayfish muscle fibers (*6*), frog spinal ganglion cells (*7*), toad spinal motoneurons (*8*) treated with quaternary ammonium ions, squid giant axon after injection of tetraethyl-ammonium (*9*), and nodes of a toad nerve fiber exposed to heavy metal ions (*10*).

It has been found that a premature termination of the prolonged spike potential can be obtained by stimulating the inhibitory fiber to the receptor with a single shock (Fig. 1). The effect is similar to that observed when an anodal pulse is applied to the cell. Strychnine, therefore, did not block the inhibitory synaptic processes, at least not under the conditions of our experiment. Finally, it was found that when calcium ions were added to the extracellular fluid the duration of spike potential became normal.

The spatial pattern of electrical activity during the plateau of the intracellularly recorded spike has been studied by recording with an external microelectrode along the surface of the axon and the cell body (see *11*). The site of origin of the spikes has been found, in agreement with the results of Edwards and Ottoson (*11*), to be in the axon, several hundred microns away from the soma. Only the first spike of the burst invades the soma, as indicated by record *B* of Fig. 2. It would seem that the sustained depolarization of the soma spreads to the axon, causing its repetitive firing. Whether the oscillations recorded in the soma eventually participate in the process of initiation of the spike in the axon is still to be ascertained.

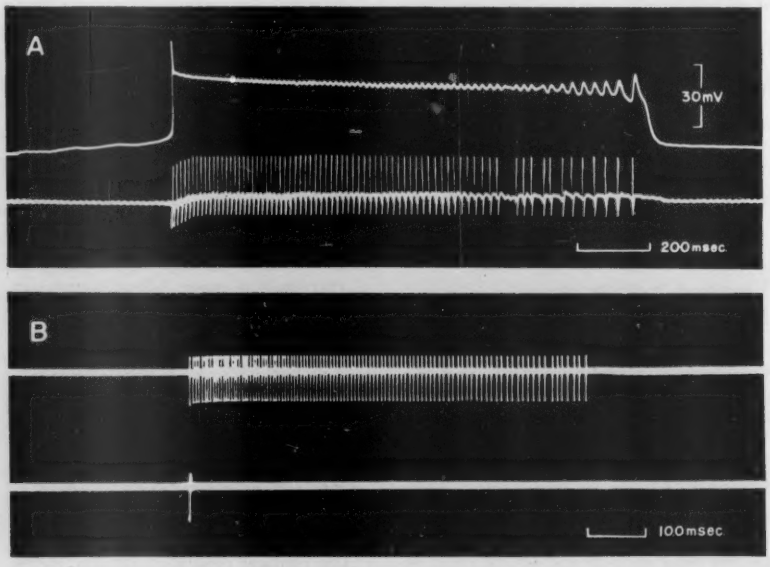

Fig. 2. (*A*) Intracellular record from the soma (upper trace) and extracellular record from the axon (lower trace) after application of strychnine. (*B*) The upper trace shows the discharge of impulses from the axon, while the lower trace is a microelectrode recording from the outside of the soma membrane. Note that inward current (down deflection) occurs in the soma only during the first spike of the burst.

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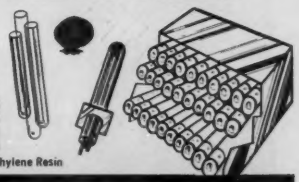

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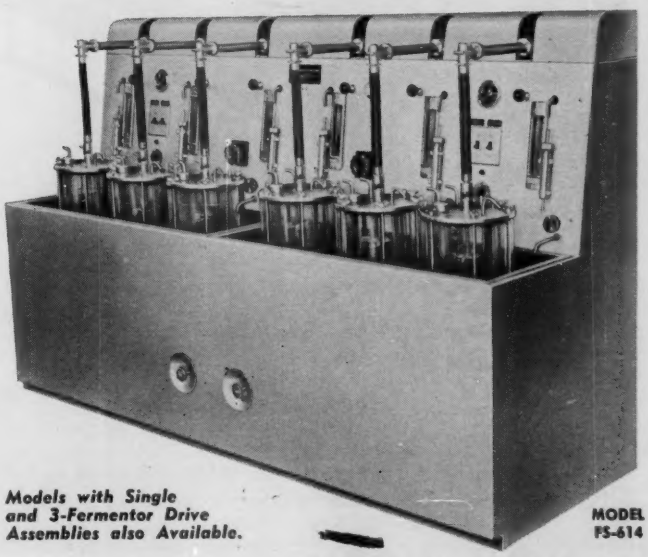

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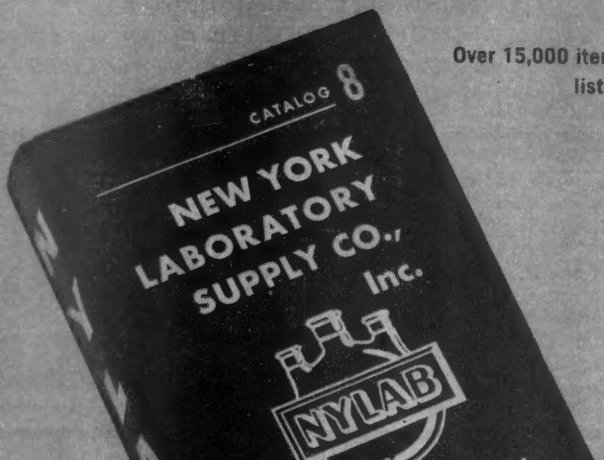

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26–2. American Inst. of Mining, Metallurgical, and Petroleum Engineers, annual, St. Louis, Mo. (AIME, 29 W. 39 St., New York 18)

27–3. Conference on Analytical Chemistry and Applied Spectroscopy, 12th, Pittsburgh, Pa. (L. P. Melnich, U.S. Steel Corp., Monroeville, Pa.)

March

1–3. Chemistry Symp., intern. (by invitation), Stanford, Calif. (B. Lamar, Stanford Univ. News Service, Stanford, Calif.)

2–4. Optical Soc. of America, spring meeting, Pittsburgh, Pa. (Miss M. Warga, 1155 16th St., NW, Washington 6, D.C.)

2–5. National Wildlife Federation, 25th annual, Washington, D.C. (Natl. Wildlife Federation, 1412 16th St., NW, Washington 6)

5–9. Gas Turbine Conf. and Products Show, 6th annual, Washington, D.C. (Meetings Dept., American Soc. of Mechanical Engineers, 29 W. 39 St., New York 18)

6–8. North American Wildlife and Natural Resources Conf., 26th, Washington, D.C. (C. R. Gutermuth, Wildlife Management Inst., 709 Wire Bldg., Washington 5)

7–9. American Railway Engineering Assoc., annual, Chicago, Ill. (N. D. Howard, 59 E. Van Buren St., Chicago 5)

8–10. Instrument Soc. of America Conf., 11th annual, Pittsburgh, Pa. (R. R. Webster, 900 Agnew Ave., Pittsburgh 30)

8–11. Neurosurgical Soc. of America, Boca Raton, Fla. (R. K. Thompson, 803 Cathedral St., Baltimore 1, Md.)

9–10. Magnetohydrodynamics, symp. on engineering aspects of, Philadelphia, Pa. (N. W. Mather, Project Matterhorn, P.O. Box 451, Princeton, N.J.)

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13–17. National Assoc. of Corrosion Engineers, annual, Buffalo, N.Y. (W. A. Mapler, 18263 W. McNichols Rd., Detroit 19, Mich.)

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14–16. Clinico-Pathological Significance of Renal Biopsy, Ciba Foundation symp. (by invitation only), London, England. (Ciba Foundation, 41 Portland Place, London, W.1)

14–16. Inter-Station Supersonic Track Conf., 6th symp., China Lake, Calif. (U.S. Naval Ordnance Test Station, Code 307, China Lake, Calif.)

15–17. Medical Photography and Cinematography, intern. cong., Cologne, Germany. (Deutsche Ges. für Photographie, Neumarkt 49, Cologne)

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20–24. American Surgical Assoc., Boca Raton, Fla. (W. A. Altemeier, Cincinnati General Hospital, Cincinnati 29, Ohio)

20–24. National Health Council, forum and annual meeting, New York, N.Y. (NHC, 1790 Broadway, New York 19)

20–24. Western Metal Cong. and Exposition, 12th, Los Angeles, Calif. (A. R. Putnam, American Soc. for Metals, Metals Park, Ohio)

21–23. American Meteorological Soc., general meeting, Chicago, Ill. (E. P. McClain, Dept. of Meteorology, Univ. of Chicago, Chicago 37)

21–23. American Physical Soc., Division of High-Polymer Physics, 21st, Monterey, Calif. (D. W. McCall, Bell Telephone Laboratories, Murray Hill, N.J.)

21–23. American Power Conf., 23rd annual, Chicago, Ill. (W. C. Astley, Philadelphia Electric Co., 900 Sansom St., Philadelphia 5, Pa.)

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26–29. American Assoc. of Dental Schools, annual, Boston, Mass. (R. H. Sullens, 840 N. Lake Shore Dr., Chicago 11)

27–31. Temperature—Its Measurement and Control in Science and Industry, natl. symp., Columbus, Ohio. (C. M. Herzfeld. Natl. Bureau of Standards, Washington 25)

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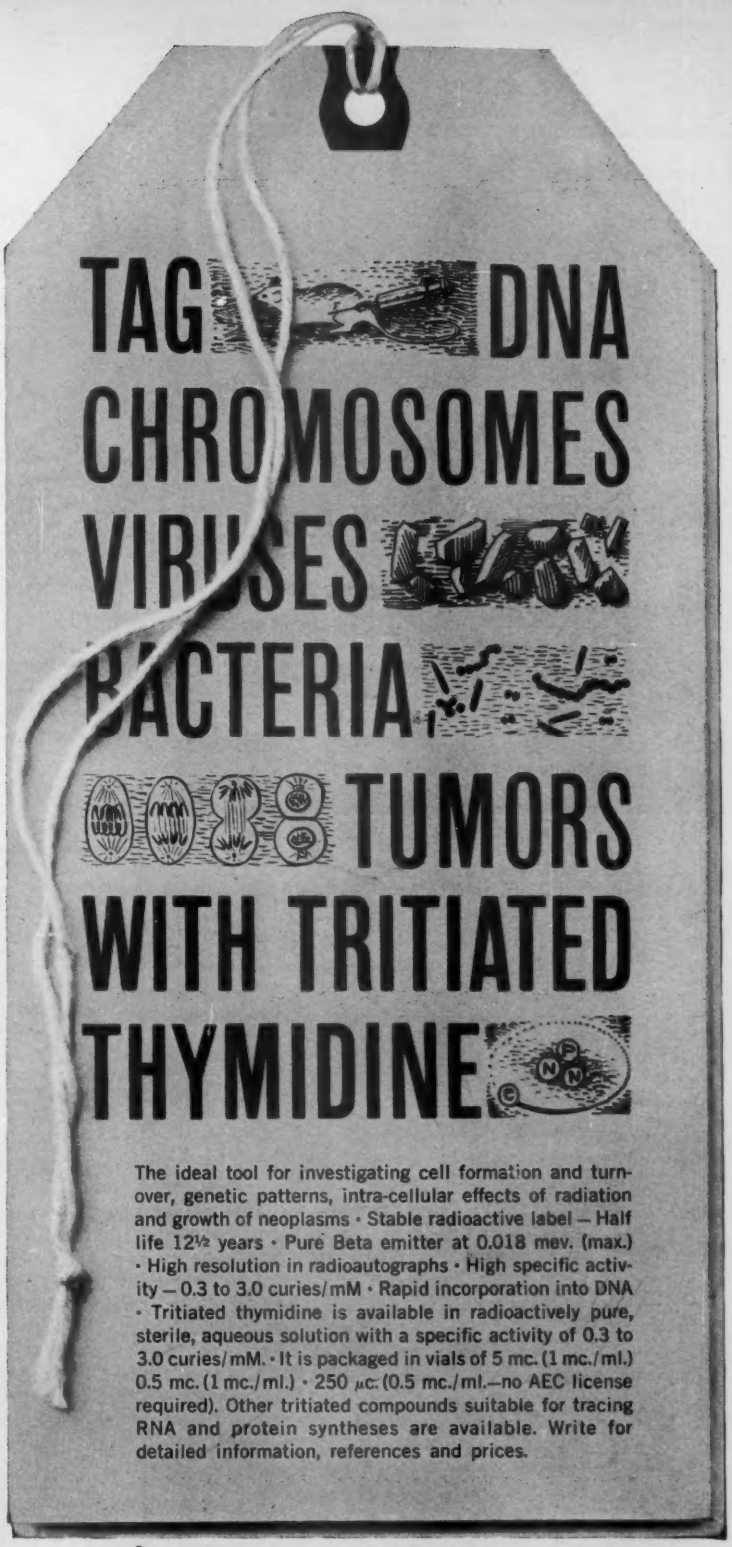

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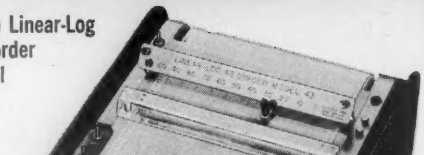

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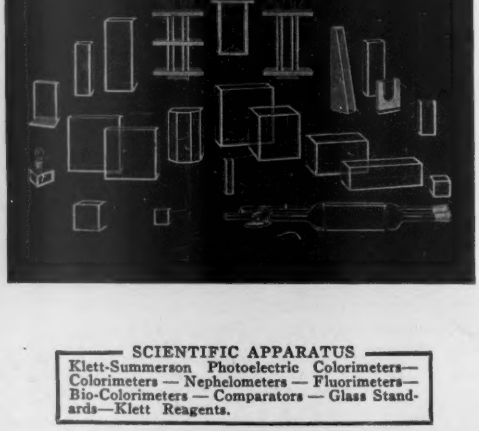

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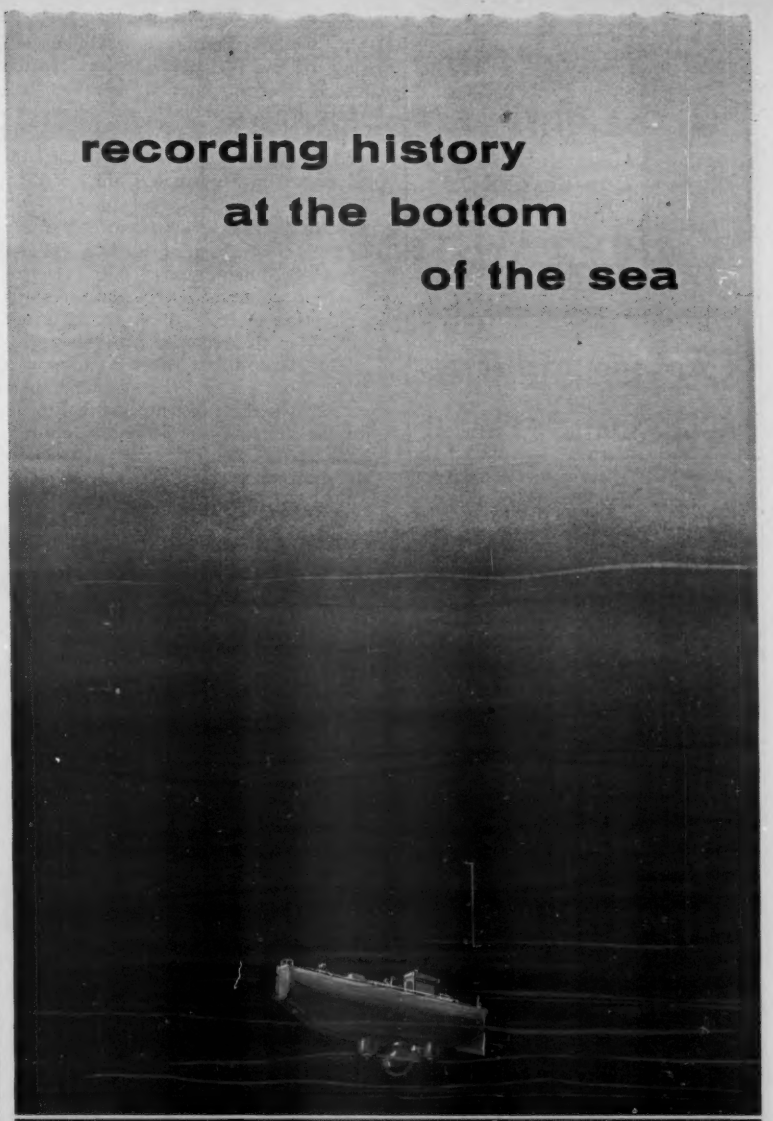
Time constant of the tube is 1 μsec; over-all frequency response is static to 5 kcy/sec. Output signal is 10 volts full scale at 150 ohms. Spectral response is S11, 3000 A to 7000 A with peak at 4400 A. Noise of the photocathode is 10^{-16} amp/cm^2 at 22°C. The tube is 5 in. in diameter and 18 in. long; the tracker measures 10 by 12 by 24 in. (Optron Corp., Dept. Sci70, 335 S. Salinas St., Santa Barbara, Calif.)

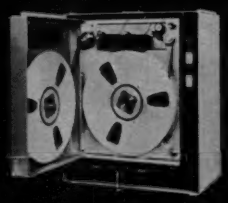
■ STEREOTAXIC INSTRUMENT is designed to make it possible to conduct experiments on small dogs, such as beagles, terriers, and others weighing 10 kg or less, where cranial regularity can be found. Other models now in use in the field can be sent to the manufacturer for modification for use with small dogs. (H. Neuman & Co., Dept. Sci74, Skokie, Ill.)

■ DIGITAL CLOCK provides a visual display of 4, 5, 6, or 7 digits and contact closure outputs. Timed pulses are generated in the clock by a synchronous motor-operated switch. A mercury relay drives all of the time-generating rotary stepping switches. Contact closure outputs may be either parallel



Far below the surface, in a sealed steel ball on the *Trieste* bathyscaph, a new chapter in undersea history is being recorded—on magnetic tape. Operating in an environment of 99% relative humidity, a high-performance instrumentation tape recorder captures a permanent record of depth, temperature, ambient noise, and voice.

The recorder, Precision Model PS-207 as shown at right, was modified for the application by Lockheed Aircraft Corporation, Sunnyvale, Calif., and supplied by them to the Naval Electronics Laboratory, San Diego, for the *Trieste* installation.



For details on Precision PS-200 series analog and digital recorders for other applications, write:

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or series. A push button for each display window permits independent setting of each digit, a rotary switch selects readout interval, and an "advance inhibit" prevents any change in displayed time during a readout cycle. (Datex Corp., Dept. Sci79, 1307 S. Myrtle Ave., Monrovia, Calif.)

■ ULTRAVIOLET ANALYZER SYSTEM for automatic analysis of flowing effluent from chromatography and electrophoresis columns detects and records absorption at 2537 A. A record event marker in the recorder provides correlation between test tubes containing a relevant sample and the indicated chart record. The three instruments that make up the system—an ultraviolet absorptiometer, a recorder, and a fraction collector—can also be used independently. (LKB Instruments Inc., Dept. Sci69, 4840 Rugby Ave., Washington 14, D.C.)

■ DIGITAL COMPARATOR accepts digital information as input and compares it with preset high and low tolerance limits at rates said to be as high as 100,000 comparisons per second. Appropriate limits for each measurement are transferred to high- and low-limit registers from a tape reader or other programming device. Visual output indicators and electrical output signals to operate a printer or control circuitry are available. Solid-state circuitry is used throughout. Power requirement is 1 amp at 15 volts. (Leach Corp., Dept. Sci71, Compton, Calif.)

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■ RECORDER-CONTROLLER of round-chart type is a two-pen potentiometric instrument said to be accurate within ±0.25 percent. Minimum scale span is 1 mv d-c; available response times are 4, 10, and 24 sec, full scale. Scale length is 27.5 in.; chart speeds are 1, 8, 12, and 24 hr, and 7 days. (General Electric Co., Dept. Sci77, Schenectady 5, N.Y.)

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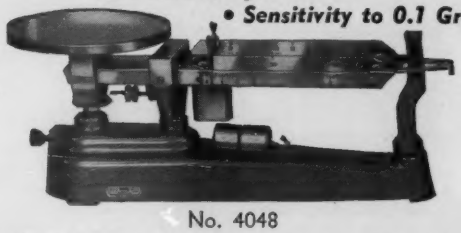

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```
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R = 10 ⑤
F = 60 ⑤
L = .2 ⑤
FOR E = 100(50)300 BEGIN ⑤
FOR C = .00002(.0000001).000021 BEGIN ⑤
I = E/SQRT(R ↑ 2 + (6.2832 * F * L — (1/(6.2832 * F * C))) ↑ 2) ⑤
PRINT (FL) = E ⑤
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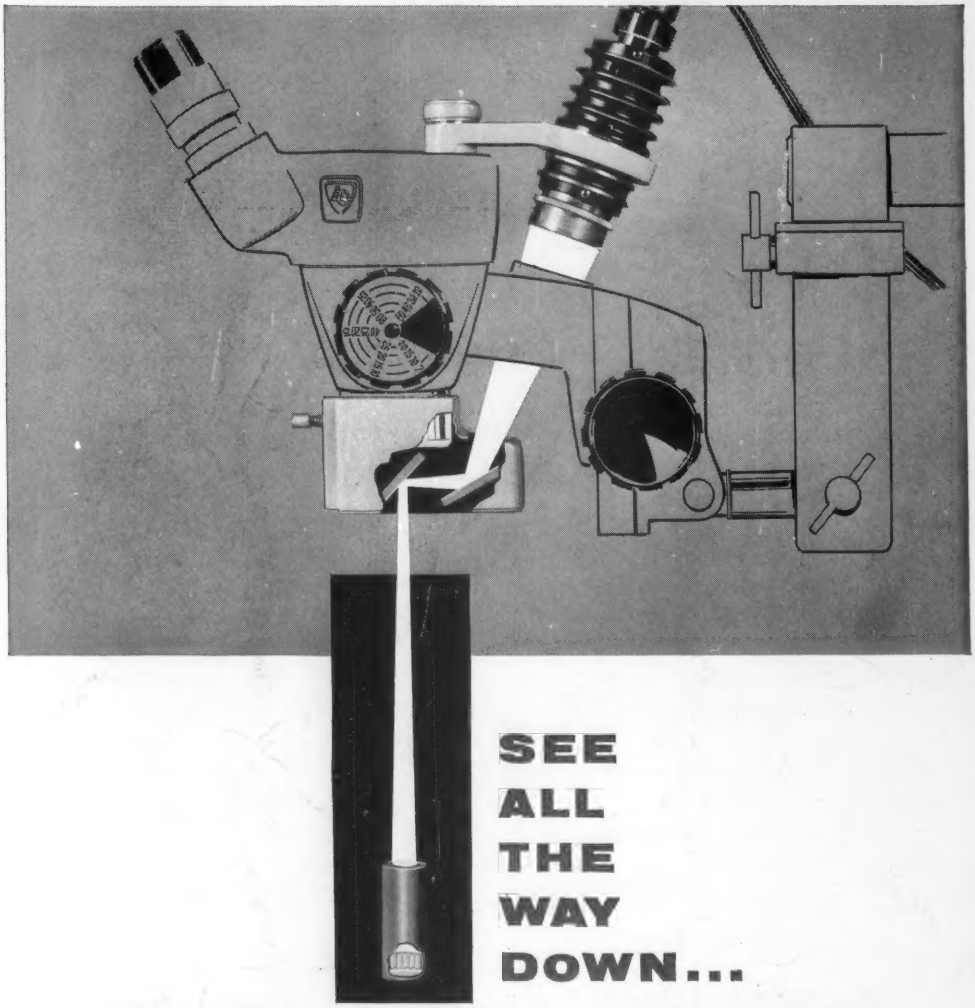

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